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OSTEOCHONDRITIS ISCHIOPUBICA IN CHILDHOOD

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In recent years it has been demonstrated that deviations from the normal process of development may occur at certain centers of bone growth in childhood. These changes have been found to take place in the first decade or two of life, before epiphysial ossification has taken place, and may consist of gross irregularities in development, of arrest in normal processes or even of retrogressive changes in the osteochondral portion of the epiphysis of certain bones.

Perthes' disease, involving the head of the femur, Osgood-Schlatter disease, with epiphysial changes in the tibial tuberosity, and vertebral osteochondrosis are classic examples of the osteochondral changes referred to and have been grouped under the head of juvenile epiphysitis or osteochondropathy.

The exact cause of such osteochondral lesions is not known, but apparently they are primary and should be distinguished from acute and chronic epiphysial lesions which are secondary to pathologic processes occurring elsewhere in the body. Trauma has been suggested as a possible cause, especially the pulling and straining of the muscle-bone structure during violent exercise. Careful search of histories, however, has failed to reveal evidence of such injuries in many of the cases recorded.

Clinically, true osteochondritis juvenilis or osteochondrosis does not resemble the inflammatory bony lesions, with their sudden onset, high temperature, local reaction of tissue, sequestration and suppuration. It shows few of the features present in infectious lesions, other than tuberculous and syphilitic, involving bone tissue.

Odelberg,[1] reporting 3 cases in which there were lesions resembling those of juvenile osteochondritis, found no evidence of bacteriologic invasion in examination of the material obtained from the affected parts during operation.

Read before the Chicago Pediatric Society, Dec. 21, 1937.

1. Odelberg, A.: Acta chir. Scandinav. **56**:273, 1924.

On the other hand, Phemister and his co-workers,[2] in 1930, reported a green-producing organism cultured from cases of Legg's disease, of Köhler's disease of the tarsal scaphoid and of Kienböck's disease of the carpal semilunar bones. Pease,[3] in 1934, reported the culture of organisms closely resembling Streptococcus viridans in a case of Osgood-Schlatter disease.

In consideration of the fact that these epiphysial lesions occur only in childhood, and in the light of more recent knowledge concerning the functions of the anterior lobe of the pituitary gland and the effect of both its growth hormone and its gonadotropic hormone on the time of closure of the epiphyses, it has been suggested that endocrine factors may play a part in the production of such lesions.

Since the clinical course of osteochondrosis in practically all the cases reported has been so favorable that operative procedure was not justified, pathologic examination of tissue has been impossible. So far as pathologic changes can be defined by means of the roentgen rays during the course of the disease, the outstanding features seem to be primarily decalcification, rarefaction and the production of cystic areas of absorption in the part affected, with possibly bone death. Later in the disease, and this may be after weeks or months, there is evidence of recalcification, increased density and apparent bone regeneration.

Roentgenologically, it may be difficult to differentiate osteochondrosis from tuberculosis, especially in early stages. Rarefied areas near epiphysial junctions are always suspicious, but the tuberculous process is more diffuse, and local changes in tissue, with thickening of the soft parts, are common. Evidence of tuberculous foci elsewhere in the body may be necessary to establish a diagnosis of tuberculosis.

The osteochondritis or epiphysitis of congenital syphilis manifests itself in early infancy and not at the age at which the cases of osteochondritis just described occur. Syphilis of the bones producing such destructive changes is rarely seen in later childhood, and when present it is accompanied by other evidence of syphilis. Roentgenologically, syphilitic lesions of bone are characterized by thickening, condensation and hypertrophy rather than by atrophy. Multiple pathologic conditions of bone and periosteal thickening are usually found. Careful physical examination and serum reactions should clarify the diagnosis.

In 1924, Van Neck [4] described 5 cases of osteochondritis in which lesions appeared at the junction of the ischium with the pubis. Subse-

2. Phemister, D. B.; Brunschwig, A., and Day, L.: Streptococcal Infections of the Epiphyses and Short Bones: Their Relation to Köhler's Disease of the Tarsal Navicular, Legg-Perthes' Disease and Kienböck's Disease of the Os Lunatum, J. A. M. A. **95**:995 (Oct. 4) 1930.

3. Pease, C. N.: Am. J. Surg. **24**:149, 1934.

4. Van Neck, M.: Arch. franco-belges de chir. **27**:238, 1924.

quently, other papers described cases closely paralleling those of Van Neck. In 1932, Heeren [5] reported that roentgenologic evidence of lesions of the ischiopubic junction appeared in 33 instances in a series of 95 cases of roentgenograms taken of pelves of children ranging in age from 2 to 12 years. These were classified as cases of osteochondritis of the Van Neck type. In many cases with roentgenologic evidence of changes, no clinical symptoms were present, and in other cases there were only insignificant symptoms.

Other authors have reported cases of ischiopubic osteochondritis with severe focal symptoms and general manifestations entirely at variance with the manifestations of osteochondrosis juvenilis as seen in other parts of the bony structure. The question naturally arises as to whether such cases are true instances of osteochondropathy juvenilis with lesions and symptoms of greater degree and severity, or whether the condition constitutes an entirely different disease.

Recently Zeitlin [6] reported 4 cases of involvement of bone and cartilage in children 6 or 7 years of age; in 3 of the cases he designated the condition osteochondrosis ischiopubica and in 1 he called it osteochondritis ischiopubica. In October 1937, Durham [7] reported 5 cases of abnormal ischiopubic conditions, with characteristic symptoms, occurring in children whose ages average about 7½ years. These he also called cases of osteochondritis ischiopubica.

In general, the symptom complex described by most authors is essentially the same, varying only in degree. There is pain on the affected side, radiating toward the hip, into the groin and toward the knee. In some cases, the pain has been severe enough to interfere with locomotion. Pain has been present in some instances even when the patient was at rest and has often been accompanied by muscular spasm, especially by spasm of the adductor muscles on the affected side. Tenderness along the descending ramus of the pubis was reported in some cases, but tenderness in the hip joint was absent.

The temperatures reported varied from normal to hyperpyrexia. Toxemia has not been emphasized. A moderate polymorphonuclear leukocytosis has been reported in some cases, with counts up to 20,000.

REPORT OF CASES

The cases herewith presented have come under my personal observation during the last six years, so that I have had adequate opportunity to note their progress.

CASE 1.—G. P., a boy aged 9 years, had complained of a slight pain in the region of the right hip for three days previous to the time I saw him. On examination on the fourth day of his illness, I found him confined to bed with such

5. Heeren, J.: Röntgenpraxis **4**:123, 1932.
6. Zeitlin, A. A.: Radiology **27**:722, 1936.
7. Durham, H. A.: J. Bone & Joint Surg. **19**:937, 1937.

severe pain in his right leg that he was unable to stand on it. The limb was held slightly flexed and somewhat adducted. Extreme tenderness was present along the inner side of the thigh from the inguinal region to the knee, tapering off in sensitivity toward the knee. There was a spasm of the adductor muscles on this side, especially on passive motion of the limb or on deep palpation. There was no tenderness about the pubic bones, the hip joint or the ischium.

No elevation of temperature was present at this time. Results of the general examination were negative. Two weeks previously, the boy had been confined to bed with a sore throat, but he had completely recovered. He had been playing a good deal of baseball, and, in the absence of other pathologic conditions, a diagnosis of muscle strain, tendon strain or "charleyhorse" was made.

After three days the pain was so severe that the affected side could be moved only with the greatest care and the child was unable to sleep at night without a sedative; the temperature rose irregularly to 101 F. There was tenderness along the descending ramus of the pubis and about the ischiopubic junction.

Suspecting osteomyelitis, I had a blood count made, which showed 10,000 leukocytes and 71 per cent polymorphonuclears. A roentgenogram showed lesions characteristic of osteochondrosis. Three days later the pain disappeared, and it was impossible to keep the child at rest. He was examined after a six month interval and found to be normal in every respect.

CASE 2.—J. B., a boy aged 8 years, was taken sick with pain in the upper part of his left leg three days before I saw him. No elevation of temperature was present at the onset. The second day slight fever developed, and the pain was so severe that passive motion was resisted. Since this attack occurred during the season for poliomyelitis, a tentative diagnosis of that disease had been made when I saw him on the third day of his illness.

There was such severe tenderness about the ischiopubic junction and the adjoining tissues that the child screamed when moderate pressure was applied. The adductor muscles were in a state of spasm, and the leg could not be moved. The white count was 11,000; the spinal fluid, obtained by puncture, was normal, and the reflexes were normal. A roentgenogram taken two days later showed the rarefactive changes at the ischiopubic junction which are associated with osteochondropathy.

It is significant, perhaps, that this child also had been suffering from a "cold" and "sore throat" for several days previous to the time I saw him and had, in fact, a diffuse "red throat" at the time of examination.

A week after the onset the pain disappeared, and a month later the boy was normal. Unfortunately, no follow-up roentgenograms were taken.

CASE 3.—H. K., a boy aged 6½ years, complained of listlessness and slight fever, with some pain in the right leg on walking. I saw him on the third day of his illness and made the following observations: A distinct limp was present on walking, the leg being held somewhat flexed and adducted. There was no tenderness at the hip or along the bony part of the pelvis, but there was some tenderness down the inner side of the right thigh, with the greatest intensity at the adductor tendons.

The next day the tenderness was more extreme and a temperature of 102 F. was present. Adductor spasms developed and the child remained in bed of his own volition.

On the fifth day the fever subsided, and the parents consented to hospitalize the child. The white cell count of the blood was 16,000, with polymorphonuclear leukocytes constituting 81 per cent of the total; the calcium content was 11 mg. per hundred cubic centimeters and the phosphorus content 7.2 mg. Roentgeno-

grams of the ischiopubic synchondrosis showed a condition of rarefaction or decalcification at the anatomic junction of the inferior pubic ramus and ischium on the right side (fig. 1). There was no periostitis and no extension of the process beyond the site of the synchrondrosis.

After eight or nine days, the pain disappeared and it was difficult to keep the child quiet. Roentgenograms (figs. 2 and 3) taken at intervals from the onset, January 1937, to September 1937 show the apparent progression in decalcification with later recalcification or regeneration and healing. The final report by the roentgenologist, nine months after the onset, states: "Stereoscopic roentgenograms taken in the anteroposterior view reveal the ischiopubic synchrondrosis within normal limits as to density and outline, although there is some apparent increase in size and thickness as compared to the left side."

CASE 4.—H. J., a boy aged 8 years, entered the hospital Dec. 8, 1937, complaining of pain in the left groin and hip. Four days before admission, he

Fig. 1 (case 3).—*A*, roentgenogram taken Jan. 18, 1937, showing areas of decalcification or rarefaction at the right ischiopubic junction. *B*, roentgenogram taken Feb. 1, 1937, demonstrating how the extension of decalcified areas in the right ischiopubic region gave rise to a moth-eaten appearance.

had fallen on the ice and been kicked in the left groin. Except for the momentary pain at that time, there had been no symptoms until two days later. The father stated that the child had complained of pain in this region one month previously but had not mentioned it again until the present time.

Examination gave negative results except for moderate generalized adenopathy with some painful nodules in the left groin, pain on passive rotation of the left leg and tenderness over the left ischial tuberosity. The temperature was 100.4 F., and the white count 11,350.

A roentgenographic examination showed decalcification at the ischiopubic synchondrosis on the left side, with a triangular promontory extending into the obturator foramen. At the synchondrosis on the right side there was evidence of some degree of decalcification, with the formation of a slight promontory extending into the obturator foramen on the right.

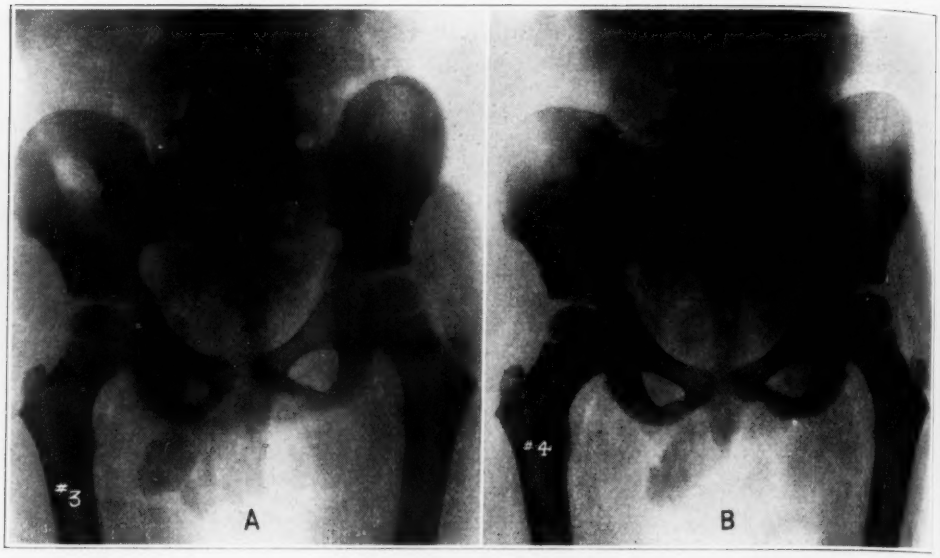

Fig. 2.—*A*, roentgenogram of March 1, 1937, showing areas of beginning recalcification or regeneration in the midst of the dystrophic portion of the right ischiopubic region. *B*, roentgenogram taken April 4, 1937, showing marked increase in the density of the right ischiopubic region, especially at the junction of the synchondrosis with the adjoining bone.

Fig. 3.—*A*, roentgenogram of June 3, 1937, illustrating an almost complete repair of the previously decalcified area, with a density apparently exceeding that of the unaffected side. *B*, roentgenogram taken Sept. 27, 1937, showing a normal right ischiopubic synchondrosis with the exception of the serrated-appearing inferior margin. The previously affected side appears thicker and more dense than the unaffected side.

Two days after the boy's entrance, the temperature rose to 102 F. and the white count was 16,000. Four days after admittance, the temperature dropped to 99 F., and it remained low. Pain gradually disappeared.

COMMENT

Roentgenologically, the condition in these cases resembles that previously described under the term osteochondritis or osteochondrosis ischiopubica and also conforms to the descriptions of osteochondrosis juvenilis as seen in other parts of the bony structures.

Clinically, the degree of pain manifested and the intensity of the focal symptoms were unlike those seen in other osteochondral lesions, i.e., Perthes' disease or Osgood-Schlatter disease. In the latter, the pain or tenderness felt was insignificant, considering the destructive changes shown in the roentgenogram. However, it must be remembered that little or no pain was present in the cases here presented after the acute symptoms had subsided, although destructive changes could be demonstrated by means of the roentgen rays for several weeks after apparent onset.

It therefore seems possible that the lesions of the synchondrosis may have been present for some time before they gave rise to any subjective symptoms, and that the acute pain and tenderness occurred only after an already disturbed or diseased tissue had been further irritated, either by trauma or by infection. Under the circumstances, it might be rational to name the forms in which there are minor symptoms and classic roentgenologic lesions osteochondrosis and those in which there are acute symptoms osteochondritis.

Zeitlin [6] made the following distinction in naming the roentgenologic-pathologic picture. In osteochondrosis the process of decalcification and dystrophy is strictly localized in the synchondrosis, with normal-appearing or slightly condensed bone on the side of the ischium and of the pubis at their junction with the decalcified area. The affected focus remains in this condition for several weeks or months; then the process of restitution begins. The condition in which the decalcification and dystrophy are not limited to the ischiopubic junction he calls osteochondritis ischiopubica. There is extension of the process to the adjoining bone, forming one continuous focus. Such involvement is likely to continue for months or years, with, however, relatively mild clinical symptoms.

Zeitlin mentions also the characteristic projection of a bony cartilaginous mass into the obturator foramen. In cases of ischiopubic disease, this promontorium reaches such size as to be incompatible with the small mass sometimes seen in normal ossification.

SUMMARY

Although pathologic changes affecting the bony structures ordinarily belong to the field of orthopedics, the pediatrician is called on to make the primary diagnosis of the relatively uncommon juvenile forms of osteochondropathy. The differential diagnosis of ischiopubic osteochondritis concerns chiefly simple trauma, the acute and subacute types of osteomyelitis, tuberculosis and syphilis. The most important factors in determining the diagnosis are the onset with rapidly progressive local manifestations, the relatively mild accompanying symptoms and the characteristic roentgen picture.

The prognosis is favorable, requiring only rest of the parts affected, and no cases have been reported of permanent disability following this form of osteochondritis.

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BASAL ENERGY METABOLISM AND CREATININE IN THE URINE

II. PREDICTION OF BASAL HEAT PRODUCTION FROM CREATININE

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In a previous communication,[1] one of us reported simultaneous measurements of the rate of excretion of creatinine and of total heat production in an attempt to clarify some of the difficulties an investigator encounters when dealing with the basal metabolism of children of unusual body build. It has been established that the rate of excretion of creatinine can be used as a measure of the active protoplasmic mass, because it is generally accepted to be an index or measure of the weight of the body musculature.[2] The muscles represent a predominant and nearly constant proportion of the total active protoplasmic mass in the body. In another study, based on 37 lean, normal, obese and emaciated children,[2a] we have shown that there may be marked variations in the amount of musculature in children of the same weight but of different body build. The weight of muscles as calculated from the output of creatinine constituted 25 per cent of the body weight of obese children and 55 per cent of that of lean children. Moreover, our studies led us to conclude that weight and height are not always an accurate index or measure of the musculature. While most children of normal weight for height appeared to have average muscular development, we found that a few showed an excessive accumulation of subcutaneous tissue in relation to the underlying musculature, both by inspection and by measurements of the creatinine coefficient (*i. e.*, milligrams of creatinine excreted per kilogram of body weight). Likewise, we found other children who were of normal weight but who were relatively lean. These unpredictable differences in

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1. Talbot, N. B.: Basal Energy Metabolism and Creatinine in the Urine: I. Observations on Children, Am. J. Dis. Child. **52**:16 (July) 1936.

2. (*a*) Talbot, N. B., and Broughton, F.: The Measurement of Obesity by the Creatinine Coefficient, Am. J. Dis. Child. **55**:42 (Jan.) 1938. (*b*) Talbot.[1]

body build may account for some of the difficulties associated with the standards of metabolism based on height and weight. If the difficulties are due to differences in the amount of musculature, it should be possible to overcome them by using standards based on the excretion of creatinine in the urine.

The present series is comprised of 63 measurements on 15 normal boys and on 27 normal girls. Included in the normal group are 47 measurements on 23 children of a private school,[3] obtained in connection with a study of school children conducted by several departments of Harvard University. The ages of the children ranged from 7 years to 14 years 11 months. There are measurements on 10 apparently normal hospitalized children whose ages ranged from 1 year 8 months to 12 years 7 months, and there are 8 measurements on 8 children 6 years old,[3] obtained in connection with a study of normal infants and young children being conducted by the department of child hygiene of the Harvard School of Public Health. The total number of observations now reported comprise a group which is sufficient to indicate the importance of using the excretion of creatinine as a standard of reference for the evaluation of basal heat production.

METHODS

The methods used in the estimation of the total calories (*i. e.*, the twenty-four hour basal heat production) and of the excretion of creatinine are, except in one instance, the same, as the methods outlined in the previous papers.[2] In the case of the infant, the total calories were measured by the cot calorimeter method at the Massachusetts General Hospital.[4] The measurements of the present series and also those of the earlier series [1] of 15 children studied by us and of twenty-five adults reported by other workers are compared and recorded graphically in the chart.

COMMENT

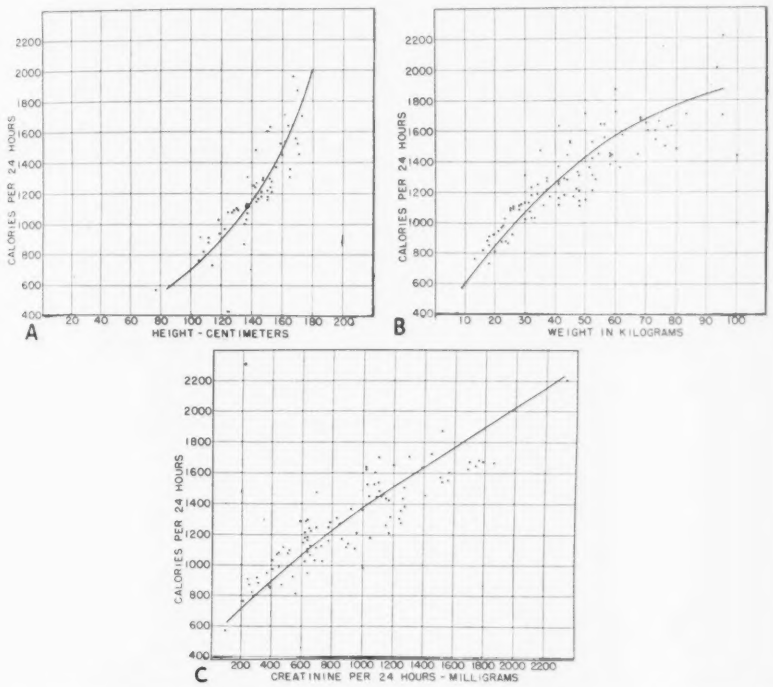
It is generally recognized that the total calories of most average normal children may be predicted within statistically defined limits from either their height or their body weight.[5] The correlations between total calories for twenty-four hours and height in the series are protrayed in curve *A*, and the correlations between calories and weight, in *B*. That a similar correlation exists between total calories and the twenty-four

3. The measurements made on these children were parts of more extensive studies provided for by a grant of the General Education Board.

4. With the cooperation of Dr. Harold Higgins.

5. Talbot, F. B.; Wilson, E. B., and Worcester, J.: Basal Metabolism of Girls: Physiologic Background and Application of Standards, Am. J. Dis. Child. **53**:273 (Jan., pt. 2) 1937.

hour excretion of creatinine is demonstrated in *C*. These three curves show clearly that the mutual relation between total calories and creatinine is approximately as accurate as that between total calories and either height or weight. It follows as an obvious corollary that the number of milligrams of creatinine excreted in a period of twenty-four hours may be used for the prediction of normal heat production in the same manner that weight and height have been used in the past. Furthermore, basal metabolic rates (the percentage deviation of total calories above or below an average normal mean) may be found



A, shows correlations between height and heat production per twenty-four hours; *B*, between weight and calories per twenty-four hours; *C*, between creatinine per twenty-four hours and calories per twenty-four hours.

by comparison with the curve which represents the average of the observations.

If the excretion of creatinine is to be used as a standard from which the normal basal metabolism may be predicted, it is important that the excretion of creatinine remain unaltered as an index or measure of the body musculature when the heat production is altered by thyroid. That this is so has been substantiated by Thorn,[6] Pugsley, Anderson and

6. Thorn, G. W.: Creatine Studies in Thyroid Disorders, Endocrinology 20:628, 1936.

Collip,[7] Poncher, Visscher and Woodward,[8] Kepler and Boothby,[9] and by studies on patients whom we have observed and will report on later. It would appear, therefore, that the rate of excretion of creatinine is essentially as stable a measurement as either height or total body weight. Consequently, excretion of creatinine should be a serviceable standard of reference for the evaluation of basal heat production.

Although the three curves show that the total calories of the average child may be predicted with approximately the same accuracy from the height, the weight or the excretion of creatinine, it does not necessarily follow that the metabolic rates derived from the three standards of reference will be the same for an individual child. An analysis of the metabolic rates of the present series shows that there may be decided differences between the rates based on these standards. A thyrotoxic girl observed by us[10] serves to illustrate this point. Her metabolic rate before treatment was +39 per cent by height, +56 per cent by weight and +70 per cent by creatinine. One of these three metabolic rates must conform more closely to the clinical status than the other two. It remains for future clinical investigation to demonstrate which standard gives results that agree most closely with the condition of the individual patient.

Observations concerning the basal metabolic rates of children of abnormal body build and with disturbances of the glands of internal secretion are being conducted in an endeavor to relate the meaning and the clinical significance of the determined metabolic rates in such children.

CONCLUSION

This additional information on the excretion of creatinine and basal energy metabolism suggests that creatinine may be used as a standard of reference for the prediction of normal heat production. The creatinine standard appears to be as satisfactory as the previous ones, and in some respects it further clarifies the physiologic significance of heat production.

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7. Pugsley, L. I.; Anderson, E. M., and Collip, J. B.: The Effect of Thyrotropic Hormone and of Desiccated Thyroid upon Creatine and Creatinine Excretion, Biochem. J. **28**:1135, 1937.

8. Poncher, H. G.; Visscher, M. B., and Woodward, H.: Creatine Metabolism in Children with Hypothyroidism, J. A. M. A. **102**:1132 (April 7) 1934.

9. Kepler, E. J., and Boothby, W. M.: Creatinuria in Hyperthyroidism, Am. J. M. Sc. **182**:476, 1931.

10. F. C., 6 years and 10 months old. Her measurements were: height 129 cm.; weight, 21.4 Kg.; excretion of creatinine per twenty-four hours, 234 mg., and total calories, 1,380.

SECOND ATTACKS OF POLIOMYELITIS

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REPORT OF A CASE

R. S., a 20 year old woman was admitted to the contagious disease division of the City Hospital on Nov. 29, 1933, and was discharged on Nov. 25, 1934. She was readmitted Dec. 15, 1934, and died Jan. 5, 1935.

Past History.—The patient had poliomyelitis in 1916, at the age of 3 years, after which she was operated on several times by orthopedic surgeons in New York city. Her muscles had become sufficiently strong for her to walk without support, though with a limp. The bones of the leg, but not those of the foot, had grown to the normal length.

Present Illness.—On Nov. 1, 1933, the patient felt weak and complained of gas on her stomach, of heartburn and of constipation. She had anorexia and vomited green bile-like material. Laxatives and enemas were of no avail. A physician prescribed magnesium sulfate, but this did not give results. Two days later, he washed out the stomach; still the bowels did not move. The pain in the abdomen became so severe that the patient was admitted to another hospital. There the bowels finally became open, and she was sent home. On November 15, a cold in the head developed. A few days later, there was difficulty in urination, and in a few more days paralysis of all the muscles of both legs developed.

Physical Examination.—On admission, the patient was semistuporous and at times delirious. She had obvious paralysis of the muscles of both legs; the deep reflexes in both lower extremities were absent; those in the upper extremities were sluggish, and the superficial abdominal reflexes were missing. The temperature was 37.2 C. (99 F). There were 13 cells in the clear spinal fluid; the pressure was 12 mm. of mercury, and the reaction to the Pandy test was 4 plus. The patient became less stuporous after the lumbar puncture.

Progress.—On December 15 both arms were almost completely paralyzed and the patient had drenching sweats. By Jan. 5, 1934, she was extremely emaciated. She could talk only in a whisper. On January 14 there was slight improvement in the movements of the hands and shoulders. Hydrotherapy was started four days later. On February 22 pyelitis developed, and the patient's temperature ranged from 37.5 to 38.5 C. (99.5 to 101.3 F.). She gradually improved and by May 9 could move the upper extremities and had started to move the thighs. On June 24 she had a gastrointestinal upset which lasted two days. By October 6 there was atrophy of the muscles of both legs. The muscles of the feet were functionless, the patient being unable to flex or to extend either foot. There was some function in all the muscle groups of both thighs. The extensors were the weakest, their function being from 30 to 40 per cent of normal; the rest of the muscles had from 60 to 80 per cent of normal function. The patient could stand alone by balancing herself and locking the knees in hyperextension. She was unable to walk without support. There was good function of the back and of the abdominal muscles. She was able to sit up and to bend without support.

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There was considerable atrophy of the intrinsic muscles of both hands; nevertheless, she was able to manage her personal needs. The deltoid muscles were normal, and the muscular function of both arms and forearms was from 60 to 80 per cent normal. On discharge, on Nov. 25, the young woman was referred to the orthopedic and the physical therapy department.

After her discharge, the patient remained well until December 11 when she had another attack of abdominal distention. The following day her legs felt heavy and ached. On December 13 she was nauseated, had anorexia and vomited. She had no bowel movement from this time until December 15 and did not void for twenty-six hours previous to that date.

On December 15 the patient was readmitted to the hospital. She was poorly nourished but did not appear ill. The temperature was normal. The condition of the muscles was the same as it had been on discharge save that the weakness of the legs was slightly greater. About two weeks later, during a small epidemic in the ward, an influenzal infection developed. The weakness of the muscles gradually became worse, and by Jan. 1, 1935, the hands, the feet and the legs were paralyzed. The temperature went up to 38.5 C. (101.3 F.). The paralysis became general. On January 4 signs of bronchopneumonia developed. At this time all the muscles of the arms and legs were paralyzed save those of the shoulder. The intercostal muscles became paralyzed. The patient died suddenly the next morning, respirations ceasing before the pulse stopped. An artificial respirator was used to no avail. The temperature at no time had been above 38.5 C. (101.3 F.).

Autopsy.—Death occurred at 3:50 a. m. An autopsy was performed at 9:20 a. m. the same day by Dr. Heitzman of the laboratory of pathology. His observations were as follows: bronchopneumonia, bilateral and slight; edema of the lungs; chronic cholecystitis; degeneration in the ventral and the lateral corticospinal tract and unilateral degeneration of the ventral born; atrophy of the muscles of the lower extremities; chronic rheumatic heart disease, with mitral valvulitis; moderate duodenal dilatation; small cortical adrenal adenomas; primary calcified tuberculous complex of the left lower lobe of the left lung and bifurcation nodes; bilateral deformity of the second and third toes, and a surgical scar over the left ankle and the right thigh. The culture of blood from the heart showed no growth.

For special examination, the sympathetic ganglions in the thoracic region on the left side at approximately the head of the fourth rib were removed down to the second and third lumbar regions, together with the overlying pleura. Several of the spinal ganglions were removed. The right sciatic nerve, together with portions of the lumbar and the sacral plexus was removed, and the sciatic nerve was followed down to the region of the midthigh. The cord and the brain were taken out en bloc and sectioned.

On microscopic examination no significant changes were detected in either the sympathetic or the spinal ganglions. The number of axis-cylinders in the sciatic nerve was reduced, and there was an increased amount of connective tissue in the endoneurium. The nerve bundles showed varying degrees of severe degeneration. A section taken through the upper portion of the lumbar region of the cord revealed extensive degeneration in the ventral corticospinal tracts bilaterally and in both lateral corticospinal tracts. The leptomeninges showed no significant changes. One anterior horn failed to show the presence of ganglion cells.

The distinctive feature of the case was the fact that although the patient was completely paralyzed there were absolutely no signs of acute inflammation in the spinal cord, suggesting, of course, that some other condition must explain the paralysis.

COMMENT

Still [1] reported a case in which a second attack of poliomyelitis occurred and reviewed 8 others described in the literature. Since his article was written, 8 more cases have been added, making 17 in all. The case described in this paper would be the eighteenth on record, since in all particulars it was similar to those noted in other reports. Yet I do not feel that this case was an instance of a bona fide second attack of poliomyelitis. I postulate my objections on the theory that a person who has had poliomyelitis is a prey not so much to another attack of the same disease as to other diseases, such as influenza, measles and scarlet fever, which involve the few remaining peripheral nerve fibers and their cells of origin. Years ago I described a case of poliomyelitis [2] in a patient who had recovered completely and who a few weeks later suddenly succumbed to an attack of bronchopneumonia. At the time I was impressed with the fact that the autopsy showed such great loss of nerve cells, only a few anterior horn cells being left in some sections, and that nevertheless these few cells were capable of carrying on complete function. The mother stated that the child had become completely paralyzed when pneumonia developed, but her observation was dismissed at the time with unbelief. Thus a striking feature of this case was missed. Obviously, if in this child the few remaining neurons and their viable strands had become involved by any peripheral or central nerve toxin (such as influenzal toxin), paralysis would recur and the clinical picture apparently would be that of a second attack of poliomyelitis. Several cross infections of scarlet fever and of so-called influenza have occurred among our patients with poliomyelitis. During the acute stages of these unrelated infections weaknesses of the previously involved muscles usually developed again. It has been shown experimentally [3] that monkeys with old poliomyelitis and with residual fixation atrophies will become paralyzed again if given an acute infection.

If the few viable fibers remaining after an attack of poliomyelitis are affected by other toxins or poisons and a toxic neuronitis (synonyms: disseminated encephalomyelitis, toxic encephalomyelopathy, peripheral neuritis, etc.) or some such condition results, the objective picture of the second attack is paralysis. Should such a thing be possible, the number of proved cases of second attacks of poliomyelitis is small indeed. With the case reported here, there are 18 in the literature. I

1. Still, G. F.: Arch. Dis. Childhood **5**:295, 1930.

2. Toomey, J. A., and Lipson, H. A.: A Case of Poliomyelitis, Am. J. Dis. Child. **41**:1389 (June) 1931.

3. Toomey, J. A.: Second Attacks of Experimental Paralysis Produced by Measles Pneumonia in Monkeys, to be published.

believe the subsequent paralyses in this case were the result of influenza affecting the few remaining nerves and cells. Harmon and Harkins [4] mentioned 2 cases but gave no details. Neal's 2 cases [5] lack pertinent facts relative to the illness. Moore's case [6] can be ruled out, since the child became paralyzed after an attack of measles. The same picture is easily reproduced in experimental animals. The patient in Cohen's [7] first case had paralysis in 1908, and after an infection of the gallbladder on Sept. 2, 1933, paralysis again developed. So much time had elapsed between the time of the attack and the time when the patient was first seen by Cohen (Jan. 5, 1934) that one cannot be sure the condition was not the result of another infection at the time of the illness in September. Cohen's second case, that of E. K., whose original attack occurred in October 1916, may have been a second attack. However, here too a slight acute infection, this time of the throat, was present. This fact does not rule out poliomyelitis. The patient was ill from Nov. 1, 1934, to November 12 or 13, when she had virtual quadriplegia. The patient in Quigley's [8] case in 1931 had poliomyelitis, in June 1933 mild pertussis, on July 17 a mild infection of the upper respiratory tract and on July 27 a sore throat and difficulty in talking—a succession of infections, plus bronchopneumonia. As in another case, which I plan to report subsequently, the spinal cord was "mushroomed," and intensely congested and tortuous, especially in the lumbar area. Most significant of all was the fact that there was incipient axonal degeneration of the recurrent laryngeal nerve, and in a few places there was phagocytosis. Certainly, despite the presence of cuffing about the vessels, this case could have been one of toxic neuronitis in a person who had an old poliomyelitis.

One can agree with Taylor [9] that the cases of Auerbach, Neurath, Lovegren, Sinkler, Friedjing and Hennelly should be excluded, since in no instance did the "second" attack occur more than four months after the first.

In reviewing the cases cited by Still,[1] one should immediately rule out that of Sanz.[10] The patient, a woman, had her first attack at the

4. Harmon, P. H., and Harkins, H. N.: The Significance of Neutralizing Substances in Resistance and Recovery from Poliomyelitis, J. A. M. A. **107**:552 (Aug. 22) 1936.

5. Neal, J. B., in Poliomyelitis: A Survey Made Possible by a Grant from the International Committe for the Study of Infantile Paralysis, Baltimore, Williams & Wilkins Company, 1932.

6. Moore, T.: Brit. M. J. **2**:166, 1934.

7. Cohen, L.: New England J. Med. **213**:601, 1935.

8. Quigley, T. B.: Second Attacks of Poliomyelitis: Review of the Literature and Report of a Case, J. A. M. A. **102**:752 (March 10) 1934.

9. Taylor, E. W.: J. Nerv. & Ment. Dis. **44**:207, 1916.

10. Sanz, F.: Rev. Neurol. & Psychiat. **13**:544, 1915.

age of 1 year, and her second when 15 and was seen by Sanz for the first time only *twenty years later,* when she was 35. Obviously, nothing could be known about the second attack; it would be impossible to rule out a peripheral neuritis of some sort. The history of Cadouin's [11] case was not available. In Taylor's [9] case a boy had paralysis at the age of 3 years, the right leg and left arm being afflicted. A second attack occurred about three years later, but the boy was not seen by Taylor until 15 months afterward. The history states that he had headache, fever and questionable convulsions, improved for several days, then again had fever, slept restlessly and finally one day awakened with virtual quadriplegia. No dates are available, and the history is scanty. Although the child had extensive paralysis, the author states that "he was unable to walk for six months," thus inferring that the boy could walk after six months—a history more like that occurring after toxic neuronitis. The patient of Francis and Moncriff,[12] D. R., was 18 years of age and had had poliomyelitis at 3 years. About Feb. 21, 1918, after gymnastic exercises, she became ill, onset being insidious, with general malaise, and with pain in the lumbar region and in the lower extremities. This patient also had had catarrhal rhinopharyngitis with mild fever lasting from four to five days. Eight days after the onset, she suffered complete loss of power in the left lower extremity and partial loss of power in the right lower extremity. There were 80 cells in the spinal fluid. Here again there is a history of an acute infection and reinfection, which occurred in February, out of the season for poliomyelitis.

Still's patient [1] was a 7½ year old girl who at 21 months had had poliomyelitis. On Sept. 30, 1929, she stumbled in walking and fell, although she did not hurt herself badly. On October 1 she had pain in the back of the neck, was feverish and sweated. She was in bed three days and on October 5 showed signs of paralysis. This looks like a true case of a second attack, and yet one cannot rule out the effect of trauma. A 33 year old woman (M. C.) admitted to the division of contagious diseases of our hospital had severe poliomyelitis, became better and was actually walking with the aid of crutches and executing good movements of locomotion. She became impatient and requested discharge from the hospital. She had been home but a week when she stumbled, fell and twisted her ankle. She went to bed, and the paralysis returned to the legs and the feet in such extreme degree that she was never able to walk again.

In 1910, the patient (R. H.) of Lucas and Osgood [13] had poliomyelitis with residual paralysis of the dorsal flexors of both feet and of the

11. Cadouin, cited by Still.[1]

12. Francis, F. D., and Moncriff, W. F.: J. Nerv. & Ment. Dis. **49**:273, 1919.

13. Lucas, W. P., and Osgood, R. B.: Transmission Experiments with the Virus of Poliomyelitis, J. A. M. A. **60**:1611 (May 24) 1913.

peroneal groups of the right leg. In September 1912, he had bronchitis and coryza; his right arm became weak, the weakness in the affected legs increased, and he had fever. He recovered, and on November 8 his condition was about the same as it had been when he was attacked. His sister had poliomyelitis about the same time.

Recently it has been shown [14] that Macacus rhesus monkeys which had survived a mild attack of experimental poliomyelitis after the injection of a weak strain of virus were protected when given a second minimal paralyzing dose of a weak heterologous strain, although they might have a second attack of the disease when given a minimal paralyzing dose of a virulent heterologous strain. Monkeys which had survived a severe attack after the injection of a minimal paralyzing dose of a virulent strain of virus never had the disease after another dose of either a homologous or a heterologous strain of virus, although the disease might again develop if they were given multiple minimal paralyzing doses of either homologous or heterologous strains of highly virulent virus. Protection thus seemed relative, not absolute, and the experiments suggest quantitative rather than qualitative differences in strains of virus.

In the experiments just referred to, poliomyelitis was produced in such an artificial manner that results can hardly be applied to the epidemiologic study of the disease in human beings. One may admit the possibility, but not necessarily the probability, that in a patient who has recovered from poliomyelitis and who is subsequently exposed to massive doses of virus the disease may again develop.

CONCLUSION

It would seem that although second attacks of poliomyelitis may occur, their number is few. It cannot be positively stated that the case reported here or many cases described in the literature are instances of a second attack of poliomyelitis. All that can be said is that these are cases in which the patient had previous attacks of poliomyelitis and subsequent attacks of paralysis. In the presence of any acute infection, such as influenza, bronchopneumonia, measles, coryza due to the virus of the common cold or scarlet fever, or in the presence of an injury, one has a right to question the diagnosis of a second attack of poliomyelitis and to insist that toxic neuronitis be first ruled out. If acute infections do aggravate the clinical condition of an old poliomyelitis, as has been shown experimentally, few of the reported cases in the literature can qualify as actual instances of a second attack of poliomyelitis.

14. Toomey, J. A.: J. Immunol. **35**:1, 1938.

IRON DEFICIENCY IN PREGNANT RATS

ITS EFFECT ON THE YOUNG

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Little information is available concerning the effect of iron deficiency during pregnancy on the iron content and blood hemoglobin content of the young. Fetzer,[1] in 1913, determined the iron content of rabbits born to females receiving high and low iron diets. His results, although not entirely conclusive, showed a correlation between the female's intake of iron and the iron content of the young. In rats it has been repeatedly demonstrated that animals of the second generation fed a diet deficient in iron show anemia during the early weeks of life.[2] A few determinations of the hemoglobin level at birth have revealed normal values. Similar observations have been reported for mice[3] and for pigs.[4] These studies do not present conclusive evidence in favor of congenital deficiency of iron, because the young received iron-deficient diets during a period of active growth. Parsons and others[5] have

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1. Fetzer, M.: Studien über den Stoffhaushalt in der Gravidität nach experimentellen Untersuchungen des Verhaltens trächtiger Tiere und ihrer Früchte bei eisenreicher und eisenarmer Ernährung, Ztschr. f. Geburtsh. u. Gynäk. **74**:542, 1913.

2. (*a*) Happ, W. M.: Occurrence of Anaemia in Rats on Deficient Diets, Bull. Johns Hopkins Hosp. **33**:163 (May) 1922. (*b*) Scott, M. D. S.: Studies in Anaemia: II. Comparison of Methods of Producing an Anaemia Characterized by a Low Color Index, Biochem. J. **17**:166, 1923. (*c*) Mitchell, H. S., and Schmidt, L.: The Relation of Iron from Various Sources to Nutritional Anemia, J. Biol. Chem. **70**:471 (Oct.) 1926. (*d*) Parsons, L. G., and Hickmans, E. M.: Studies in the Anaemias of Infancy and Early Childhood: II. The Effect of Yeast on Nutritional Anaemia in Rats, Arch. Dis. Childhood **8**:95 (April) 1933.

3. Schmidt, M. B.: Ueber die Organe des Eisenstoffwechsels und die Blutbildung bei Eisenmangel, Verhandl. d. deutsch. path. Gesellsch. **15**:91, 1912.

4. McGowan, J. P., and Crichton, A.: Iron Deficiency in Pigs, Biochem. J. **18**:265, 1924.

5. Parsons, L. G.; Hickmans, E. M., and Finch, E.: Studies in the Anaemia of Infancy and Childhood: XI. The Effect of Iron Deficient Diets on the Size of the Red Blood Cells in Rats and in the Production of Microcytic Hypochromic Anaemia in Their Offspring; a Contribution to the Study of Congenital Iron Deficiency Anaemia in the Human Infant, Arch. Dis. Childhood **12**:369 (Dec.) 1937.

recently reported a depression of the hemoglobin value at birth in the third generation of rats fed with iron-deficient diets.

There has been little agreement as to the effect in man of maternal iron deficiency on the hemoglobin of the young. The various theories may be summarized as follows: The blood of infants born to mothers with iron deficiency may have (1) a low hemoglobin content at birth and during the first year,[6] (2) a normal hemoglobin content at birth but anemia may occur during the first year,[7] or (3) a normal hemoglobin content at birth and during the first year.[8] The first two theories presuppose the presence of congenital deficiency of iron. The only quantitative studies pertaining to this problem were performed by Toverud.[9] She determined the iron content of the livers of infants dying shortly after birth and found slight decreases in 8 of 12 infants born to anemic mothers.

In order to obtain more detailed information regarding the effect of maternal iron deficiency on the young the present study was undertaken. Determinations of the iron content and studies of the blood were made for young rats born to females which received an iron-deficient diet during pregnancy. The results, in general, show that iron deficiency in the mother leads to iron deficiency in the young.

PROCEDURE

Nulliparous albino rats of the Wistar strain, aged from 5 to 7 months, were used for mating. These rats had been raised on a stock diet of two-thirds whole wheat (containing 1 per cent of iodized sodium chloride) and one-third whole milk powder. They had also received weekly supplements of fresh vegetables and liver. Each female was placed in a self-emptying glass cage with a male, and both received an exclusive diet of whole milk powder (klim) and distilled water ad libitum. Repeated analyses of samples of milk powder were made for iron by the method of Hanzal[10] and for copper by the method of Elvehjem and

6. (*a*) Parsons, L. G.: Congenital Anaemia: A Contribution to the Study of Nutritional Anaemia, Acta pædiat. **13**:378, 1932. (*b*) Neale, A. V., and Hawksley, J. C.: Studies in the Anaemias of Infancy and Early Childhood: VI. Nutritional Anaemia in Mother and Child, Arch. Dis. Childhood **8**:227 (Aug.) 1933.

7. (*a*) Mackay, H. M. M.: Nutritional Anaemia in Infancy, with Special Reference to Iron Deficiency, Medical Research Council, Special Report Series, no. 157, London, His Majesty's Stationery Office, 1931, p. 63. (*b*) Strauss, M. B.: Anemia of Infancy from Maternal Iron Deficiency in Pregnancy, J. Clin. Investigation **12**:345 (March) 1933.

8. Fullerton, H. W.: The Iron-Deficiency Anaemia of Late Infancy, Arch. Dis. Childhood **12**:91 (April) 1937.

9. Toverud, K. U.: Investigation on the Iron Store of Newborn Infants, Acta pædiat. (supp. 1) **17**:136, 1935.

10. Hanzal, R. F.: Determination of Iron in Biological Material, Proc. Soc. Exper. Biol. & Med. **30**:846 (April) 1933.

Lindow.[11] There was no significant variation in the samples used.[12] The males were removed from the cages when the females became pregnant. When a second pregnancy was desired the males were again placed with the females after the first young had been weaned. Samples of blood were obtained from the tails of both the adult and the young rats. Erythrocyte counts were performed with the Bureau of Standards apparatus, and hemoglobin values were estimated by the Newcomer method standardized by the oxygen capacity technic. Erythrocyte-counting pipets and microcolorimeter cups were used in the determinations of the hemoglobin content. At the end of the experimental periods the mother rats were anesthetized with ether and were decapitated. After the blood ceased to flow from the vessels of the neck the liver was removed, and two separate pieces were washed, weighed, dry ashed and analyzed for iron. Determinations of the total iron content of newborn rats were made on the individual carcasses after washing and ashing. The analyses for iron were again performed by the method of Hanzal.[10] Repeated experiments during the course of the study showed this method to be satisfactory.

OBSERVATIONS ON FEMALE RATS

The average erythrocyte count, hemoglobin content of the blood, and iron content of the liver for normal female rats and the values for

TABLE 1.—*Blood Values and Liver Iron of Rats Receiving a Stock Diet and of Rats Receiving a Milk Powder Diet for Varying Periods* *

Days on Diet	Erythrocytes, Million per Cu. Mm.	Hemoglobin, Gm. per 100 Cc.	Liver Iron, Mg. per 100 Gm. Fresh Weight
0	8.7 (27)	15.5 (27)	30.2 (11)
75	6.5	12.1	25.1
240	7.7	15.3	5.2
240	8.4	14.7	8.4

* The figures in parentheses indicate the number of animals studied.

3 animals receiving milk powder for varying periods are recorded in table 1. In the latter group there was a gradual depletion of iron in the liver, but even after eight months there was no appreciable change in the erythrocyte count or the hemoglobin content of the blood.

Before describing the effect of pregnancy on milk-fed rats, it might be well to give normal blood and iron values for pregnant rats receiving a complete diet. Van Donk and others [13] found that the physiologic anemia of pregnancy became most pronounced during the four or five days before parturition. At this time the hemoglobin value averaged 11 to 13 Gm. per hundred cubic centimeters of blood and the erythrocyte count 6,000,000 to 7,000,000 per cubic millimeter. The hemoglobin

11. Elvehjem, C. A., and Lindow, C. W.: The Determination of Copper in Biological Materials, J. Biol. Chem. **81**:435 (Feb.) 1929.

12. Typical analyses of the milk powder used were: iron, 0.32, 0.36 and 0.37 mg.; copper, 0.08, 0.09 and 0.09 mg. per hundred grams.

13. Van Donk, E. C.; Feldman, H., and Steenbock, H.: An Analysis of the Anemia of Pregnancy in the Rat, Am. J. Physiol. **107**:616 (Jan.) 1934.

content returned to the normal level (15 to 16 Gm.) about twenty-one days post partum. Kojima [14] found the average iron content of the livers of nonpregnant rats to be 27.9 mg. per hundred grams of fresh weight, while at the end of pregnancy the values had decreased to 16.7 mg. In my studies I found that the livers of stock rats twenty-one days after parturition had a normal iron content.

The effects of pregnancy on rats receiving a milk powder diet, both exclusively and with supplements of copper, iron and iron and copper, are recorded in table 2. The copper was given to rule out any possible deficiency of this element. The iron was given to study its effect on the hemoglobin and iron stores of the mothers and the young.

TABLE 2.—*Effect of Pregnancy on Average Blood Values and Iron Content of Livers of Female Rats Receiving Milk Powder Diet* *

			Before Diet Was Begun		1 to 4 Days Before Delivery		21 Days Post Partum		
Series	Daily Supplement	Days on Diet Before Delivery	Erythrocytes, Million per Cu.Mm.	Hemoglobin, Gm. per 100 Cc.	Erythrocytes, Million per Cu. Mm.	Hemoglobin, Gm. per 100 Cc.	Erythrocytes, Million per Cu. Mm.	Hemoglobin, Gm. per 100 Cc.	Liver Iron, Mg. per 100 Gm. Fresh Weight
			First Pregnancy						
A	None	46 (12)	8.7	15.7 (17)	7.4	12.9 (10)	8.5	12.4 (12)	5.8 (2)
A_1	None	29 (6)	...	.....	...	.....	8.4	14.4 (6)	7.1 (4)
B	Copper 0.5 mg.†	39 (10)	8.7	15.3 (6)	7.3	11.9 (6)	7.9	12.6 (10)	5.7 (4)
C	Iron 5 mg.‡	26 (4)	8.6	15.4 (4)	6.8	11.6 (3)	7.8	14.6 (2)	25.2 (2)
D	Iron 5 mg. + copper 0.5 mg.	26 (4)	8.5	15.3 (4)	6.4	13.0 (3)	8.4	14.8 (4)	28.2 (4)
			Second Pregnancy						
A	None	107 (10)	...	.....	7.7	9.9 (10)	8.9	9.1 (10)	5.1 (7)
B	Copper 0.5 mg.	89 (4)	...	.....	7.4	11.2 (4)	9.2	8.4 (4)	5.2 (4)

* The figures in parentheses indicate the number of animals studied.
† Given as cupric sulfate (Merck, c.p.) in drinking water.
‡ Given as ferric chloride (Mallinckrodt, c.p.) in drinking water.

Some minor variations in experimental procedure should be mentioned at this time. First, in series A (first pregnancy) the female rats were given the milk powder diet for several days before the male rats were placed in the cages. All the other rats were started on the diet at the same time that the males were placed in the cages. Second, rats from series A and B were allowed to nurse some of their young after both pregnancies, while the young were removed from all other animals shortly after birth. Third, in series A (first pregnancy) samples of blood were taken from the rats repeatedly before, during and after pregnancy, whereas for rats of the other series determinations were made only as listed in table 2. The repeated sampling of the blood, together with the prolonged period of feeding with milk powder, of the rats in series A might account for the greater degree of iron deficiency observed in their young as compared with the young of the rats in series A_1 and B.

14. Kojima, K.: Das Eisen in normalen und pathologischen Geweben und seine biologische Bedeutung: IV. Untersuchungen des Eisengehaltes in verschiedenen Organen weisser Ratten während der Schwangerschaft und Solcher im normalen Zustand, Nagoya J. M. Sc. **5**:78 (March 15) 1931.

The general results for the female rats were little affected by the aforementioned variations in procedure. At the end of the first pregnancy rats receiving the milk powder diet (series A) showed no abnormal depression of the erythrocyte count or of the hemoglobin value. Twenty-one days post partum the hemoglobin content was only slightly less than normal, but the iron content of the liver had decreased to 5.8 mg. per hundred grams, or to one-fifth normal. When rats subjected to a single pregnancy were given the milk powder diet supplemented with large doses of copper, iron or iron and copper (series B, C and D), there was no appreciable difference in the erythrocyte counts and hemoglobin values from those observed for rats given the milk powder diet alone. It is apparent, however, that the livers of rats receiving iron or iron and copper had a normal iron content when studied twenty-one days post partum.

No difficulty was encountered in obtaining a second pregnancy of the milk-fed animals. Between the first and the second pregnancy the erythrocyte counts average 10,000,000 to 11,000,000 per cubic millimeter and the hemoglobin value 14 to 16 Gm. per hundred cubic centimeters of blood. At the end of the second pregnancy (series A) the average hemoglobin content was 9.9 Gm., and twenty-one days post partum, it had decreased to 9.1 Gm. per hundred cubic centimeters. This value, with the relatively high erythrocyte count, indicates the presence of anemia due to iron deficiency. Similar values were obtained for a group of rats that received copper supplements (series B, second pregnancy). The iron content of the liver for both groups averaged 5.15 mg. per hundred grams of fresh weight, which was slightly lower than that after the first pregnancy.

These results show that a single pregnancy of a rat fed with milk powder caused a decrease in the iron store in the liver without affecting the hemoglobin content of the blood. After a second pregnancy, moderate anemia due to deficiency in iron occurred.

OBSERVATIONS ON NEWBORN RATS

Observations on newborn offspring of normal female rats and of female rats with iron deficiency are summarized in table 3. The serial letters represent the offspring of females with the same serial letters in table 2. It can be seen that the average size of the litter in the different groups was similar. Observations were made on 3 newborn rats from each litter within a few hours after birth. It was found that the erythrocyte counts, hemoglobin values and total iron[15] values of

15. The total iron content of the newborn rat, as measured, does not represent an absolute value, because a sample of blood had been previously withdrawn.

(Footnote continued on next page)

litter mates checked closely. In order to obtain an approximation of the distribution of iron in the newborn rat, the iron content of the hemoglobin was calculated by the following formula:

$$\text{Hemoglobin iron in mg.} = \text{Gm. wt.} \times 0.06 \times \text{Gm. hemoglobin per 1 cc.} \times 0.00335 \times 1{,}000$$

The volume of the blood is assumed to account for 6 per cent of the body weight.[16] The factor 0.00335 is used to convert hemoglobin to its equivalent in iron, and multiplication by 1,000 converts grams to milligrams.

Subtraction of the amount of iron in the hemoglobin from the total iron content gives the value for nonhemoglobin iron, which represents for the most part the free and fixed iron in the tissues.

TABLE 3.—*Average Blood Values and Iron Content of Newborn Offspring of Female Rats Receiving Either Stock or Milk Powder Diets* *

Series	Daily Supplement, Mother's Diet	Average No. of Rats per Litter	No. of Newborn Rats Studied	Weight, Gm.	Erythrocytes, Million per Cu. Mm.	Hemoglobin, Gm. per 100 Cc.	Total Iron, Mg.	Hemoglobin Iron, Mg.	Nonhemoglobin Iron, Mg.
		First Litter: Mothers Received Stock Diet							
			18	5.03	3.1	13.1	0.254	0.133	0.121
		First Litter: Mothers Received Milk Powder Diet							
A	None	7.8 (13)	17	4.89	3.1	9.7	0.112	0.095	0.017
A_1	None	7.7 (6)	15	5.05	3.1	14.0	0.146	0.142	0.004
B	Copper 0.5 mg.	7.6 (10)	26	4.98	2.9	13.4	0.152	0.134	0.018
C	Iron 5 mg.	6.0 (3)	9	5.47	3.0	12.7	0.270	0.140	0.130
D	Iron 5 mg. + copper 0.5 mg.	7.5 (4)	12	5.59	3.3	15.0	0.285	0.169	0.116
		Second Litter: Milk Powder Diet							
A	None	7.5 (11)	20	4.59	2.1	6.6	0.071	0.061	0.010
B	Copper 0.5 mg.	6.0 (4)	11	4.54	2.2	6.9	0.072	0.063	0.009

* The figures in parentheses indicate the number of litters studied.

For the newborn offspring of female rats that received a stock diet (table 3), the total iron content averaged 0.254 mg. and was distributed about equally between the hemoglobin and the nonhemoglobin portion. For the young of the first litter (series A) born to female rats with moderate iron deficiency, the hemoglobin value was reduced about 25 per cent, while the total iron content was reduced more than 50 per

Since the erythrocyte count and the hemoglobin value were determined by drawing blood up to the 0.3 mark in the erythrocyte counting pipet and since special care was taken to lose as little blood as possible during the testing, it is estimated that the total amount of blood lost did not exceed 12 cu. mm. As this represents only about 2 per cent of the total iron content, it may, for the purposes of these experiments, be disregarded.

16. (*a*) Chisolm, R. A.: On the Size and Growth of the Blood in Tame Rats, Quart. J. Exper. Physiol. **4**:207, 1911. (*b*) Griffith, J. Q., Jr., and Campbell, R.: A Method for Determining Blood Volume in Rats, Proc. Soc. Exper. Biol. & Med. **36**:38 (Feb.) 1937.

cent. It is thus evident that the decrease in the total iron content occurred mostly at the expense of the nonhemoglobin portion. The newborn offspring (series A_1) of female rats with milder iron deficiency showed normal hemoglobin values at birth, but there was again a marked reduction in the total iron content and consequently in the nonhemoglobin iron. Administration of copper to pregnant milk-fed rats did not alter the picture in the young (series B). When female rats were given large supplements of iron or of iron and copper, the young (series C and D) were entirely protected against iron deficiency. It is of interest that there was no increase in the storage of iron in these animals. The erythrocyte counts for newborn rats of the different series described did not vary significantly.

In second litters (series A) of females receiving milk powder diets the iron deficiency was much more severe. These rats had rather marked anemia at birth (hemoglobin, 6.6 Gm. per hundred cubic centimeters), and the total iron content was decreased to almost one-fourth normal. Most of the iron present was contained in the hemoglobin portion. Copper supplements to the diet of the mother throughout the two pregnancies did not influence the results in the young (series B). Erythrocyte counts for the second litter averaged 2,100,000 per cubic millimeter. This value was considerably lower than that for the first litters.

Female rats that delivered the second litters had received the milk powder diet for three to three and one-half months. It therefore seemed possible that the picture in the young could have been related to other deficiencies of the mother in addition to the deficiency of iron. To investigate this, 4 female rats were given a milk powder diet and were placed with male rats. During the first week about 7.5 cc. of blood was removed from each female rat by cardiac puncture. The first litter newborn of 2 of these animals that delivered thirty-six and fifty-nine days after the experiment was begun showed practically the same severity of iron deficiency as the second litters, described previously. It therefore appears that the low hemoglobin and iron contents of the animals in the second litter were due exclusively to iron deficiency in the mother.

The effect of maternal iron deficiency on the newborn rat may be summarized as follows: When the mother has a mild deficiency the blood of the young at birth has a normal hemoglobin content, but there is a depletion of the iron stores. More severe deficiency of iron in the mother results in anemia in the newborn. Thus it seems that the newborn rat exhibits the same phenomenon as the adult of the species; that is, the first evidence of iron deficiency is a decrease in reserve iron, while further depletion of iron results in a decrease in the hemoglobin content of the blood.

OBSERVATIONS ON RATS WITH IRON DEFICIENCY DURING THE FIRST WEEKS OF LIFE

A number of the newborn rats of the first and second litters (series A) born of females that received a milk powder diet were observed during the suckling period (table 4). Not more than two samples of blood were taken from any single animal. Some of the rats of the first litters (series A) died during the period of observation, but the majority survived and weighed about 25 Gm.. each at the end of three weeks. The hemoglobin value, which averaged 9.9 Gm. per 10 cc. of blood at birth, increased slightly for a few days and then showed a gradual decrease to 6.4 Gm. per hundred cubic centimeters at the end of eighteen days. This does not represent pathologic anemia, as hemoglobin values of 6 to 7 Gm. per hundred cubic centimeters have been observed for

TABLE 4.—*Erythrocyte Counts and Blood Hemoglobin Content of Iron-Deficient Rats During First Weeks of Life*

	First Litter, Series A			Second Litter, Series A		
Age in Days	No. of Determinations	Erythrocytes, Million per Cu. Mm.	Hemoglobin, Gm. per 100 Cc.	No. of Determinations	Erythrocytes, Million per Cu. Mm.	Hemoglobin, Gm. per 100 Cc.
0	9	3.1	9.9	10	2.0	6.4
2	1	3.0	9.6	..	...	...
4	3	2.4	11.0	5	2.3	7.6
6	6	2.9	10.3	2	2.7	8.0
8	1	2.1	9.3	3	2.3	6.9
10	5	2.9	8.8	2	2.2	5.9
12	5	3.3	8.7	3	2.0	7.0
14	3	2.4	8.2			
16	5	3.0	7.5			
18	4	3.8	6.4			

normal rats at the age of 21 days.[17] Many rats of the second litter, which had more severe iron deficiency, died within one or two days after birth; rats of this litter rarely survived longer than ten to twelve days. Lipemia usually occurred toward the end of this time. The average hemoglobin value for this group never went much below the initial value of 6.4 Gm. per hundred cubic centimeters. The erythrocyte counts of the animals of both the first and the second litter were of no special significance.

Since these animals probably had little or no iron reserve at birth, it is suggested that the iron store in the newborn rat is not especially important for the formation of hemoglobin during the suckling period.

17. (*a*) Elvehjem, C. A., and Kemmerer, A. R.: An Improved Technique for the Production of Nutritional Anemia in Rats, J. Biol. Chem. **93**:189 (Sept.) 1931. (*b*) Fitz-Hugh, T., Jr.; Robson, G. M., and Drabkin, D. L.: Hemoglobin Production: IV. Evaluation of Therapeutic Agents in Anemia, Due to Milk Diets, Based on a Study of the Blood and Bone Marrow of Rats from Birth to Maturity, ibid. **103**:617 (Dec.) 1933.

This might be anticipated when one considers the small amount of reserve iron present at birth (about 0.1 mg.) as compared to the amount needed (about 0.5 to 6 mg.) for the rapid growth and for the formation of hemoglobin during the first three weeks of life.

COMMENT

Because of its clinical importance the application of these studies to human beings is worthy of comment. It has been shown that iron deficiency in the pregnant rat is associated with iron deficiency in the offspring. Certain factors were conducive to such a result: The female rat's diet contained a minimal amount of iron, the period of gestation in the rat is short and the weight of the litter amounts to almost 20 per cent of the mother's weight. As these conditions are not present in man, the experiments on rats are not directly applicable. It may be said, however, that congenital iron deficiency is a biologic phenomenon and, therefore, that its potential occurrence in the infant must be recognized.

The most recent and comprehensive articles on iron deficiency in the mother and child are those of Strauss [7b] and of Fullerton.[8] Strauss reported that infants born to mothers with anemia due to deficiency in iron had normal hemoglobin values at birth but showed the presence of anemia during the first year of life. This was interpreted as being indirect evidence for depletion of the iron store at birth. Fullerton found no definite relation between iron deficiency in the mother and anemia in the young. In the opinion of Fullerton and others, cited by Stearns and McKinley,[18] the iron stores at birth are much less important for hemoglobin formation than is the iron made available through destruction of hemoglobin during early infancy. If this is true it should be important for infants to have normal hemoglobin levels at birth (22 to 23 Gm. per hundred cubic centimeters).[18] It is of interest that in Strauss' series [7b] 1 of the infants born to an anemic mother had a hemoglobin value of 13.1 Gm. per hundred cubic centimeters. Also, I recently observed a woman with a hemoglobin content of 6 Gm. per hundred cubic centimeters of blood who gave birth to an infant with a hemoglobin content of 12 Gm. per hundred cubic centimeters. These 2 cases suggest that anemia due to iron deficiency in the mother may at times be related to a decreased hemoglobin value in the newborn infant. Further observations are necessary before an association between iron deficiency in the mother and that in the infant can be established.

18. Stearns, G., and McKinley, J. B.: The Conservation of Blood Iron During the Period of Physiological Hemoglobin Destruction in Early Infancy, J. Nutrition **13**:143 (Feb.) 1937.

SUMMARY AND CONCLUSIONS

Female albino rats were fed an exclusive diet of whole milk powder and were subjected to one or two pregnancies.

A single pregnancy did not cause anemia in the female rat but resulted in a marked depletion of the iron content of the liver. A second pregnancy resulted in moderate anemia due to deficiency in iron.

First litter offspring of female rats with mild iron deficiency had normal hemoglobin values at birth. There was, however, a considerable reduction in the total iron content and consequently in the iron stores of these animals.

Second litter offspring of female rats receiving the iron-deficient diet showed a decrease in the hemoglobin content of the blood at birth. The total iron content of these animals was reduced to one-fourth normal.

Iron supplements to the milk powder diet completely protected the mother and the offspring against iron deficiency

Supplements of copper to the milk powder diet, both with and without iron, did not affect the results significantly.

First litter offspring of female rats with iron deficiency did not show pathologic anemia during the suckling period.

The application of these studies to man is discussed.

Miss Elizabeth Jane, E. G. Jonaitis and W. A. Johnson gave technical assistance.

VALUE OF AN INCREASED SUPPLY OF VITAMIN B_1 AND IRON IN THE DIET OF CHILDREN

PAPER III

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In 1932, one of us (Summerfeldt[1]) reported that when a group of normal children were fed for ten weeks an increased amount of many of the protective food elements, including the vitamin B complex and iron, a marked increase in weight resulted. The protective food elements were given in the form of a special cereal,[2] which replaced the cereals ordinarily used. Similar results were obtained in an observation which extended for six months.[3] In the present paper, observations are recorded on the rate of increase in weight and the hemoglobin level of various groups of children who received either ordinary cereals or the special cereal in their diets for different periods, extending to a maximum of eighteen months. The children, who lived in a large orphanage on the outskirts of the city, were given excellent care and enjoyed a good diet. The details of the diet have already been recorded.[4] Briefly, the children received each day an average of 24 ounces (710 cc.) of milk, one or two vegetables besides potatoes and raw or preserved fruit; each week they had meat about five times and one to four eggs. In addition, they received carbohydrates in the form of bread and cereals.

In chart 1 *A* is shown the gain in weight of 12 children who received 3 ounces (85 Gm.) of the special cereal daily for one year. Thirteen

From the Research Laboratories of the Department of Pediatrics, University of Toronto, and the Hospital for Sick Children, under the direction of Alan Brown, M.D.

1. Summerfeldt, P.: The Value of an Increased Supply of Vitamin B_1 and Iron in the Diet of Children, Am. J. Dis. Child. **43**:284 (Feb.) 1932.

2. Tisdall, F. F.; Drake, T. G. H., and Brown, A.: A New Cereal Mixture Containing Vitamins and Mineral Elements, Am. J. Dis. Child. **40**:791 (Oct.) 1930.

3. Ross, J. R., and Summerfeldt, P.: The Value of an Increased Supply of Vitamin B_1 and Iron in the Diet of Children, Am. J. Dis. Child. **49**:1185 (May) 1935.

4. Ross, J. R., and Summerfeldt, P.: The Haemoglobin of Normal Children and Certain Factors Influencing Its Formation, Canad. M. A. J. **34**:155 (Feb.) 1936.

comparable children of the same sex and age (5 to 14 years) received the same good diet of the institution except that in place of the 3 ounces of the special cereal they were given 3 ounces, by dry weight, of ordinary cereals. It is seen that the children fed the diet containing the ordinary cereals gained at just the expected rate,[5] adding 5.4 pounds (2.45 Kg.) each, while the group receiving the special cereal gained much more rapidly, adding a total of 12.1 pounds (5.49 Kg.) each.

In chart 1 *B* is shown a similar observation on different groups of children extending for eighteen months. In this observation 14 children received 2 ounces (57 Gm.) of the special cereal daily, and 12 comparable children received 2 ounces of the cereals ordinarily used in the institution. Again it is to be noted that the increase in weight in the group receiving the ordinary cereals closely paralleled the expected

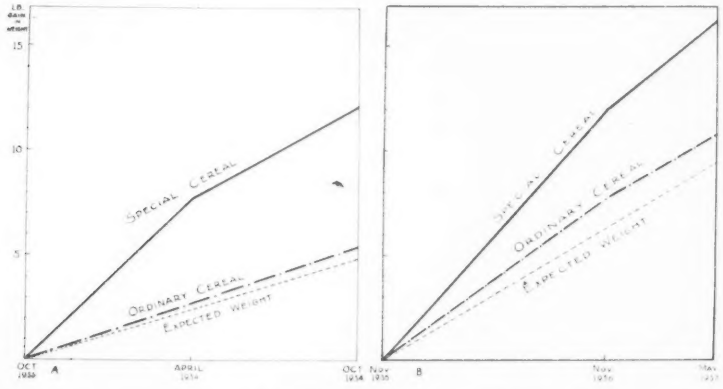

Chart 1.—*A*, comparison of the rates of gain in weight of two groups of normal children over a twelve month period. One group received a good diet containing ordinary cereals, while for the other group the ordinary cereals were replaced by an equal amount of a special cereal rich in many of the protective food elements. *B*, comparison of the rates of gain in weight of a group of normal children who received ordinary cereals and a group who received the special cereal for eighteen months.

rate of gowth, while the group receiving the special cereal gained more rapidly.

A group of 13 children receiving the ordinary good diet of the institution, which included 2 or 3 ounces of ordinary cereals each day, were observed over a period of seventeen months. At the end of this time administration of 2 ounces of the special cereal daily was begun, and the weights were taken over a period of seven months, the total period of observation being twenty-four months. The increase in

5. From the weight, height and age tables compiled from measurements of 80,000 school children in Toronto, Canada.

weight record in chart 2 *A* shows that during the seventeen months when the ordinary cereals were given the children had just the expected increase in weight, and that while the special cereal was given, during the final seven months, they gained at a markedly increased rate.

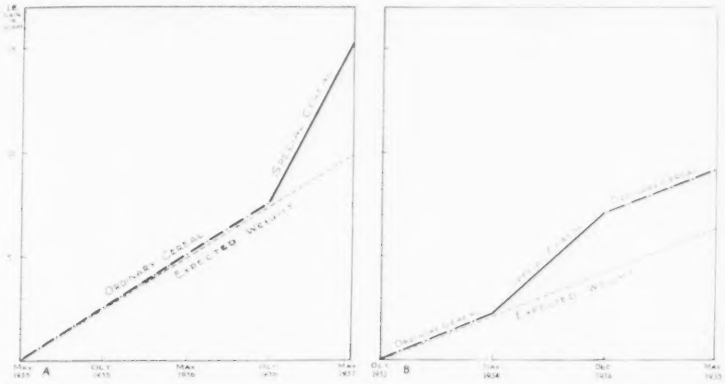

Chart 2.—*A*, comparison of the rates of gain in weight of a group of children fed ordinary cereals for seventeen months and then placed on the special cereal for an additional seven months. *B*, comparison of the rates of gain in weight of a group of children fed ordinary cereals for seven months, given the special cereal for a further seven months and then shifted to ordinary cereals for a final six months.

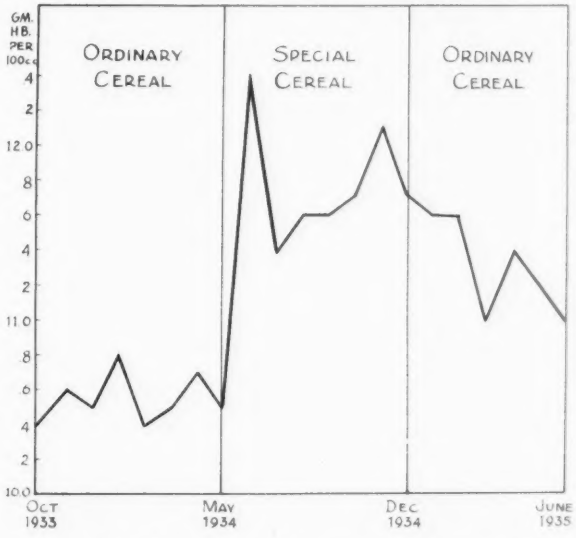

Chart 3.—Effect of feeding the special cereal on the hemoglobin level in the blood.

A final group of 19 children were observed for three periods of approximately six months each. During the first period they received each day in their diet 3 ounces of ordinary cereal; for the second period

this cereal was replaced with 2 ounces of the special cereal, while for the third period they received again the ordinary cereal, 2 ounces being given daily. In chart *2 B* is shown the definite increase in rate of growth which occurred while the children were receiving this special cereal.

The hemoglobin level of the children whose weights are recorded in chart *2 B* was determined at monthly intervals throughout the period of observation. The Newcomer method was used. The results are given in chart 3, which shows that there was a marked increase in the hemoglobin level as soon as the children were given the special cereal. During the final period, when the children were again receiving the ordinary cereal, the hemoglobin level fell at a gradual rate.

The average amount of iron obtained daily by the children in the ordinary diet of the institution during the first and third periods was calculated to be 11 mg. per day, while the use of the special cereal increased the amount to 29 mg. per day.

SUMMARY

Further evidence is presented of the effect of enriching an average good diet with additional amounts of a number of protective food elements, including the vitamin B complex and iron. As a result of this increased intake of protective food elements, the children gained weight at an accelerated rate and the hemoglobin content of the blood was increased.

CRYPTORCHIDISM TREATED WITH GONADOTROPIC PREPARATIONS

III. SURGICAL REPAIR OF CRYPTORCHIDISM WITH AND WITHOUT GONADOTROPIC THERAPY

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There have been many reports on the use of gonadotropic preparations for the correction of cryptorchidism.[1] For those patients whose condition does not respond to such therapy surgical repair has been advocated. However, few figures on a sufficiently large series of patients who have received treatment with gonadotropic preparations in combination with surgical repair are available from which to draw final conclusions.

In a previous study [2] gonadotropic extracts alone were used in treating 71 patients with 91 undescended testicles. These patients were treated with injections of the gonadotropic principle obtained from the anterior lobe of the pituitary gland and of the gonadotropic principle obtained from the urine of pregnant women. It was found that in many instances these extracts produced changes in the external genitalia, manifested by flushing of the genitalia, by enlargement of the penis and testes or by descent of the testes. In the patients treated with the gonadotropic principle of the urine of pregnant women, 48 per cent of the undescended testes completely descended, but only 45 per cent remained descended. In the patients treated with the gonadotropic principle obtained from the anterior lobe of the pituitary gland,

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The gonadotropic principles used were furnished by Parke, Davis & Co.

From the Children's Memorial Hospital and the Otho S. A. Sprague Memorial Institute. The cases of cryptorchidism in which operation was done are from the surgical service of Dr. A. H. Montgomery.

1. Bigler, J. A.; Hardy, L. M., and Scott, H. V.: Gonadotropic Principle in the Treatment of Cryptorchidism: A Review of the Literature, Am. J. Dis. Child. **55**:100 (Jan.) 1938.

2. Bigler, J. A.; Hardy, L. M., and Scott, H. V.: Cryptorchidism Treated with the Gonadotropic Principle, Am. J. Dis. Child. **55**:273 (Feb.) 1938.

25 per cent of the undescended testes completely descended, but only 18 per cent remained in the scrotum. When both extracts were used, 45 per cent of the undescended testes descended, but only 25 per cent remained descended.

Treatment seemed to be about equally successful at any age after the fourth year, but owing to the fact that enlargement of the penis was noted more often in children under 7 years of age, it was deemed advisable to postpone therapy until the seventh year of age. When descent of the testes did occur, it usually began to take place before 4,000 rat units of gonadotropic principle had been given. No atrophy of any part of the external genitalia due to the therapy with gonadotropic substance was ever observed. In a control series of untreated and inadequately treated patients with cryptorchidism, descent of the testes did not occur.

For comparison a group of 72 patients with 85 instances of cryptorchidism, treated either with surgical intervention alone or with gonadotropic therapy and operation, is presented. Forty-three patients were subjected to operation alone. Seven had operations and some time later were given a gonadotropic substance, and 22 were first treated with a gonadotropic principle and then operated on because of failure of the testes to descend completely. In most instances the operations were done by the same group of surgeons using the same surgical technic. The method of administration of the gonadotropic principle has been given in detail elsewhere.[2]

SELECTION OF PATIENTS

The 43 patients that were treated with operation only and the 7 that were operated on and treated with a gonadotropic extract had been operated on several years previous to the advent of gonadotropic therapy. They were all examined by two or more examiners on several occasions over a period of a few months to several years. There were 18 additional patients who were operated on only; they were not included in this study because of failure to return to the clinic for final examination. The 22 patients who were treated with a gonadotropic substance and then operated on were selected from our series of those who did not have complete descent of their undescended testes after receiving adequate therapy with gonadotropic extract. Eight of this group received the gonadotropic principle of the anterior lobe of the pituitary gland, 9 received the gonadotropic principle of the urine of pregnant women, and 5 received both extracts. The patients varied in age from 2 to 13 years.

HERNIA

Of the total of 85 testes subjected to operation, hernial sacs were actually found at operation to be associated with only 43, or 51 per cent. In our previous study of 96 cases 15 hernias were noted. During treatment with a gonadotropic substance hernias developed in 5 patients and 1 hernia disappeared.

EVALUATION OF RESULTS

In order to evaluate the results of operative repair, the following criteria were used: 1. A result was considered good when the testis subjected to operation was of normal size and firmness, was situated well in the scrotum and was fairly movable. 2. A result was considered fair when the testis seemed slightly smaller and firmer than normal or was fixed by scar tissue at the external ring. 3. A result was considered poor when the testis was small and atrophic and was incorporated in a mass of scar tissue. When possible, an effort was made to compare the testes as to their sensitivity to gentle pressure. Since atrophic testes have little or no sensation, it was felt that this was an adjunct in the evaluation of the postoperative condition of the testes. It is fully appreciated that one risks many pitfalls in judging from mere examination that a testis is normal or atrophic. Certainly the final answer cannot be made until these boys have been studied over a period of many years or until a time when their procreative powers are, or should be, fully developed.

RESULTS IN PATIENTS TREATED WITH OPERATION ONLY

In the group of 50 patients who were operated on without or before treatment with a gonadotropic substance, a total of 60 undescended testes were repaired; in 10 patients the operation was bilateral; 32 testes were on the right side and 28 on the left. Fourteen patients complained of pain in the region of the undescended testis before operation. The testes before operation were situated as follows: Forty-one were in the inguinal canal, 18 were not palpable, and 1 was in the perineum.

These patients were observed from one month to nine years before operation and from one month to seven years after operative repair. At the operation it was found that 4 patients had an extremely short cord holding up the testis, 2 had adhesions about the testis, 1 testis was in a reverse position and 1 was in the perineum. No unusual findings were recorded for the other patients. At operation 45 testes were reported as normal, 10 were considered smaller than normal, and 5 were considered atrophic. The results of operative repair on these 60 undescended testes were as follows: In 36, or 60 per cent, the result was good; in 12, or 20 per cent, the result was only fair, and in 12, or 20 per cent, a poor result was obtained. Eighty-two per cent of the patients could be considered as benefited by operation alone. Of the 5 testes that were considered atrophic at operation, 3 were classified as good at the final observation and 1 as fair, and 1 was removed at operation. At the final observation of the 10 testes that were considered smaller than normal at operation, results were classified as fol-

lows: 5 good, 1 fair and 4 poor. The group of 12 testes that were finally classified as showing a poor result or as being atrophic was originally made up of 7 testes that were considered normal at operation, 4 that were smaller than normal and 1 that was atrophic.

TABLE 1.—*Data on Patients Treated Only by Operation* *

Case No.	Age at Operation, Yr.	Hernia		Position of Testes		Testes at Operation		Obstruction Found at Operation		Final Result	
		R	L	R	L	R	L	R	L	R	L
1	10	No		IC		NIC		No		Fair	
2	7	Yes		IC		SIC		No		Good	
3	9	Yes	Yes	IC	IC	NIC	NIC	SC	No	Fair	Fair
4	10		Yes	IC	NP		NIC		No		Good
5	8	Yes		IC		SIC		SC		Good	
6	10		Yes	IC	IC	NIC	AIC	No	No	Good	Good
7	6	Yes	Yes	NP	NP	NIC	AIC	No	No	Good	Good
8	5	Yes		IC		SIC		No		Good	
9	7	Yes		NP	NP	NIC	AIC	No	No	Fair	Good
10	8	Yes		IC		NIC		No		Good	
11	10		Yes		IC		NIC		Sc		Good
12	8	Yes		IC	NP	NIC		No		Good	
13	10	Yes		IC		NIC		Ad		Fair	
14	12	Yes	Yes	IC	NP	NIC	NIC	No	No	Poor	Poor
15	5	Yes		IC		NIC		No		Good	
16	9			NP		NIAb		No		Good	
17	10	Yes	No	IC	NP	NIC	NIAb	No	No	Good	Poor
18	10		No		IC		NIC		Reverse		Good
19	7		Yes		IC		NIC		No		Good
20	7		No	IC	IC		NIC		No		Good
21	6	No		IC		AIC		No		Fair	
22	9	No		NP		AIC		No		Poor; testis removed	
23	5	No		NP		SIC		No		Poor	
24	11	No		IC		NIC		No		Good	
25	9	Yes		NP		NIC		No		Good	
26	12	No	No	IC	IC		NIC		No		Good
27	6		Yes		IC		NIC		No		Good
28	10	No	No	IC	IC	NIC	NIC	No	No	Good	Good
29	9		Yes		IC		NIC		SC		Good
30	10	No		IC		NIC		No		Good	
31	9		No	IC	IC		NIC		No		Poor
32	11	Yes		IC		NIC		No		Good	
33	6	No	Yes	IC	NP	NIC	NIC	No	No	Fair	Good
34	6	No		In perineum		Normal in perineum		In perineum		Good	
35	10	Yes		IC		SIC		No		Good	
36	7	No		IC		NIC		No		Good	
37	10	Yes	Yes	IC	IC	SIC	SIC	No	No	Poor	Poor
38	13	Yes		IC		NIC		Ad		Fair	
39	6		Yes		IC		NIC		No		Fair
40	7	No		IC		NIC		No		Good	
41	6	Yes		IC		SIC		No		Poor	
42	5	Yes		IC		NIC		No		Fair	
43	5		Yes		IC		NIC		No		Good

* In all tables, Ad indicates adhesions; NIAb, normal, in abdomen; NIC, normal, in canal; SIC, small, in canal; AIC, atrophic, in canal; SC, short cord; IC, in canal; NP, not palpable; AIAb, atrophic, in abdomen; G, gonadotropic principle of anterior lobe of pituitary gland (assayed at 10 to 15 rat units per cubic centimeter); A, gonadotropic principle of urine of pregnant women (assayed at 100 rat units per cubic centimeter); B, both extracts; IS, in scrotum; IS†, in scrotum part time; LC, lower part of canal; MC, middle of canal.

RESULTS IN PATIENTS GIVEN OPERATIVE REPAIR FOLLOWED BY TREATMENT WITH A GONADOTROPIC SUBSTANCE

Seven patients that had previously had surgical repair were given treatment with a gonadotropic principle. In some instances the injections were given shortly after operation and in others up to 3 years

TABLE 2.—*Data on Patients Operated on and Then Treated With Gonadotropic Substance* *

Case No.	Age at Operation, Yr.	Hernia		Findings at Operation		Results of Operation		Age at Treatment	Rat Units of Treatment	Number of Injections	Period of Treatment, Mo.	Period Observed After Treatment, Mo.	Final Result	
		R	L	R	L	R	L						R	L
44	11	Yes		NIC		Fair		12	2,870 B	37	11	9	Good	
45	8	No		SIC		Good		10	1,890 G	43	3	4	Good	
46	8		Yes		NIC		Good	8	740 G	45	5	6		Atrophy
47	6	Yes		NIC		Poor		8	1,360 B	47	11	7	Atrophy	
48	12		No		NIC		Poor	12	690 G	36	4	8		Atrophy
49	8	Yes	Yes	NIC	NIC	Good	Fair	11	825 G	40	6	6	Good	Fair
50	8	Yes		NIC		Poor		10	1,165 G	27	3	0	Atrophy	

* See footnote to table 1.

TABLE 3.—*Data on Patients Treated With Gonadotropic Substance and Then Operated on* *

Case No.	Age at Treatment, Yr.	Hernia		Testes Before Treatment		Rat Units of Treatment	Number of Injections	Period of Treatment, Mo.	Location After Treatment		Findings at Operation		Final Results	
		R	L	R	L				R	L	R	L	R	L
51	6	No		IC		635 G	34	11	IS†		NIC		Good	
52	2	Yes		IC		4,300 A	27	3	IS†		NIC		Good	
53	9		Yes		IC	2,210 B	55	5		IC		SIC		Good
54	8		Yes	IC	IC	530 G	20	3	IS	IC		SIC		Good
55	7		Yes		NP	12,165 B	94	10		NP		AIC		Atrophy
56	9	No		IC		8,035 B	76	14	IS†		NIC		Good	
57	13		Yes		IC	3,700 A	79	5		IC		NIC		Good
58	7	No	No	IC	IC	1,595 G	55	6	IC	IC	NIC	NIC	Good	Good
59	3	Yes		NP		11,580 B	82	18	IS†		NIC		Good	
60	4		Yes	IC	IC	10,600 A	46	5	IS	IC		NIC		Poor
61	6		No		NP	2,550 B	48	5		NP		AIAb		Testis removed
62	8	Yes	Yes	NP	IC	1,560 G	42	3	NP	LC	AIAb	NIC	Testis removed	Fair
63	10	Yes		IC		12,450 A	35	3	IC		AIC		Fair	
64	11		Yes		NP	11,800 A	53	7		IC		NIC		Good
65	12	No	No	NP	IC	20,250 A	57	6	NP	LC	NIC	NIC	Good	Good
66	13		Yes	IC	NP	.....	68	13	MC	NP		NIAb		Poor
67	5		Yes		NP	10,865 A	78	13		NP		AIAb		Good
68	6		No		NP	24,130 B	84	16		NP		AIAb		Atrophy
69	4	Yes		NP	IC	8,800 A	54	9	IC	IS	NIC		Good	
70	11		No		IC	1,610 G	66	7		IC		NIC		Good
71	8		No		IC	990 G	23	2		IC		AIC		Atrophy
72	3		No		NP	1,215 G	30	9		NP		NIAb		Good

* See footnote to table 1.

postoperatively. Although there were 13 undescended testes in this group of patients, there was surgical repair on only 8 of them. In 3, or 37 per cent, the result of operation was considered good; in 2, or 25 per cent, the result was thought to be fair, and in 3, or 37 per cent, there was a poor result. Therapy with a gonadotropic extract produced little or no change from the previous condition. The results were now good in 3, or 37 per cent; fair in 1, or 12 per cent, and poor in 4, or 50 per cent, the testes being atrophic. However, of 2 cases of bilateral cryptorchidism in which only 1 testis was operated on, the testis not treated with surgical intervention completely descended during treatment with gonadotropic extract in 1 and partially descended in the other. From this it would seem that adequate gonadotropic therapy was given.

In this small series treatment with a gonadotropic principle after operation did not prevent atrophy from occurring nor did it improve the condition of testes already atrophic. In 1 patient (case 46) who received regular treatment with a gonadotropic extract after an apparently successful operation the testis went on to atrophy, and in 3 patients there was no benefit to atrophic testes.

RESULTS IN PATIENTS TREATED WITH A GONADOTROPIC PRINCIPLE PLUS OPERATION

There were 22 patients with 25 undescended testes that were subjected to operation after adequate therapy with gonadotropic substance. Before operation 5 patients complained of pain in the groin, and in 5 the testes were reducible before treatment. These patients received between 990 and 24,130 rat units of gonadotropic principle over a period of from two to eighteen months. During this time 7 of the testes, or 24 per cent, partially descended into the scrotum. Four of these 7 partially descended testes did remain in the scrotum part of the time, but when treatment was stopped they again retracted into the inguinal canal, where they remained. Since no further response could be obtained from treatment with a gonadotropic principle, surgical repair of the cryptorchidism was resorted to. At operation 16, or 64 per cent, of the testes were of normal size; 2, or 8 per cent, were considered smaller than normal, and 7, or 28 per cent, were atrophic. In 8 instances there were adhesions about the testes and in 3 there was a short cord. The postoperative result was considered good in 16, or 64 per cent, and fair in 2, or 8 per cent; in 5, or 28 per cent, the testis was atrophic. In 2 cases an atrophic testis was removed at operation. Discounting the 5 testes that were found to be atrophic at operation and remained atrophic, there was a good result in 80 per cent, a fair result in 10 per cent and a poor result in

10 per cent; thus a total of 90 per cent were benefited. One of the 7 testes that were considered atrophic at operation returned to normal size after operation, 1 was classified as fair, and 5 remained atrophic. Two of those that remained atrophic were removed at operation. Both of the testes that were smaller than normal at operation developed to normal size after operation, and in only 2 instances did normal testes become atrophic after operation.

TABLE 4.—*Results According to Age*

Age at Operation, Yr.	Atrophy	Poor Results	Fair Results	Good Results	Percentage of Good Results	Percentage of Results Indicating Benefit
			In Patients Given Surgical Repair Only			
5	..	..	1	3	..	..
6	1	1	3	4	23	30
7	..	..	..	7	..	..
8	2	..	2	5	..	..
9	1	2	2	2	..	..
10	..	1	2	12	32	42
11	..	..	..	4	..	..
12	1	2	..	1	8	10
13	..	..	1	..	..	..
Total	5	6	11	38		
			In Patients Treated with Gonadotropic Principle and Operated On			
2	..	..	..	1	..	..
3	..	..	..	2	21	21
4	..	1	..	1	..	..
5	..	..	..	1	..	..
6	1	..	..	1	..	..
7	2	..	..	2	..	..
8	2	..	1	1	26	30
9	..	..	..	2	..	..
10	..	..	1	..	..	..
11	..	..	..	2	21	26
12	..	..	..	2	..	..
13	..	1	..	1	..	..
Total	5	2	2	16		

RESULTS IN RELATION TO AGE

In order to determine whether age influenced the results of treatment the patients were divided into two groups. One was composed of patients operated on and of those operated on and then treated with a gonadotropic substance, and the second was composed of those treated with a gonadotropic principle and later with operation. As shown in table 4, there was no great variation, the best results possibly occurring in patients from 7 to 10 years of age in both groups.

AGE OF PATIENTS WITH ATROPHY OF THE TESTES

Twelve atrophic testes were found at operation. The ages of the patients varied from 5 to 10 years. The age distribution of the patients was as follows: 1, 5 years; 4, 6 years; 2, 7 years; 2, 8 years; 1, 9 years, and 2, 10 years. Apparently something more than position and age was the cause of atrophy.

SUMMARY AND CONCLUSIONS

In children with cryptorchidism requiring surgical repair, slightly better results were obtained when a gonadotropic substance was given before operation than when operation alone was resorted to.

The age of the patient and the position of the testes are probably not the only determining factors among the causes of atrophic undescended testes.

Postoperative treatment with a gonadotropic principle had no beneficial effects on the testes which had been operated on, either in preventing or in correcting atrophy.

The best results seemed to occur between the ages of 7 and 10 years with all forms of treatment.

The gonadotropic principle should be given a fair trial in the treatment of cryptorchidism in boys over 7 years of age. If complete recovery does not occur after adequate therapy, operation should be considered.

RED BLOOD CELL VALUES IN ADOLESCENCE

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Adolescence is sometimes defined as that transition period between childhood and maturity in which certain significant changes occur in the physiology of the body. Several studies of the blood of youths of both sexes have shown that increases in hemoglobin values are included in these changes. We have reported [1] 640 observations on adults and on children ranging in age from birth to 13 years which contribute indirectly to such conclusions. The average values for the quantity of hemoglobin, for the number of red blood cells and for the volume of packed cells in the blood of the 12 year old children of this series are almost identical with similar values obtained for the group of women 21 to 40 years of age. There are no appreciable sex differences in the age groups up to 13 years, but in the adults the average values for men are definitely higher than those for women.

The general opinion is that the diversity of values between the two sexes begins during adolescence. The actual course of the increase which results in attainment of the adult level varies in different series. Williamson,[2] at Chicago, found no differences in the quantity of hemoglobin between boys and girls under 16 years of age. Börchers [3] found in a study of over 250 German boys between 13 and 20 years of age that adult averages for hemoglobin and red blood cells were reached in the nineteenth year. He commented on a difference in values for the two sexes during adolescence, but did not include any girls in his series. Osgood,[4] at Portland, Ore., determined the volume of packed

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1. (*a*) Mugrage, E. R., and Andresen, M. I.: Values for Red Blood Cells of Average Infants and Children, Am. J. Dis. Child. **51**:775-791 (April) 1936. (*b*) Andresen, M. I., and Mugrage, E. R.: Red Blood Cell Values for Normal Men and Women, Arch. Int. Med. **58**:136-146 (July) 1936; (*c*) Venous and Peripheral Red Blood Cell Values, Am. J. Clin. Path. **8**:46-51 (Jan.) 1938.

2. Williamson, C. S.: Influence of Age and Sex on Hemoglobin, Arch. Int. Med. **18**:505-528 (Oct.) 1916.

3. Börchers, J.: Das rote Blutbild gesunder Jugendlicher männlichen Geschlechtes im Alter von 13 bis 20 Jahren, Folia haemat. **54**:387-397 (March) 1936.

4. Osgood, E. E.: Normal Hematologic Standards, Arch. Int. Med. **56**:849-863 (Nov.) 1935.

cells as well as the quantity of hemoglobin and the number of red cells in the blood of 259 men and 152 women between 14 and 30 years of age. He observed that results for the two sexes diverged sharply at 14 years; the hemoglobin average for the girls reached the adult level at this time, while that for the boys reached the adult level about two years later. Goldhamer and Fritzell,[5] in the Great Lakes region, reported their data on 100 boys between 12 and 17 years of age. The values which they obtained were definitely lower than their accepted standards for adults.

The present study of 160 subjects between the ages of 13 and 21 years may supply some additional data on the significant, yet relatively neglected, period of adolescence.

SUBJECTS

The subjects of our series included 10 boys and 10 girls in each age group from 13 to 21 years. Of the series, 67 members had been admitted to the outpatient department of the Colorado General Hospital for correction of refractive errors and other minor disorders; 7 subjects were resident at the State Home for Dependent Children, and the remainder of the group, numbering 86, were students in high school,[6] college, medical or nursing school. All of them had been residents of Denver or its vicinity for several years. They were apparently in average health and were considered to be representative members of the general population.

METHODS

Blood was withdrawn from a cubital vein while the subject was engaged in the usual activities of the day. Either dry heparin or a mixture of ammonium oxalate and potassium oxalate (6 mg. ammonium oxalate and 4 mg. potassium oxalate to 5 cc. of blood[7]) was used as the anticoagulant. Neither of these anticoagulants in the concentration used seems to produce appreciable change in the size of the red blood cells. Hemoglobin was determined by the Van Slyke-Neill manometric measurement of oxygen capacity.[8] Wintrobe[9] hematocrit tubes were used to determine the volume of the packed cells. Red blood cell counts were made with the same degree of accuracy as in the previous studies. The details of methods and calculations are given in other publications.[1a, b]

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5. Goldhamer, S. M., and Fritzell, A. I.: A Study of the Red Blood Cell Count and Hemoglobin in the Adolescent Male, J. Lab. & Clin. Med. **19**:172-177 (Nov.) 1933.

6. Dr. A. L. Beaghler, Director of Health Service for the Denver Public Schools, and Mrs. Dorothy Lepper, R.N., assisted us materially by obtaining student volunteers from the high schools.

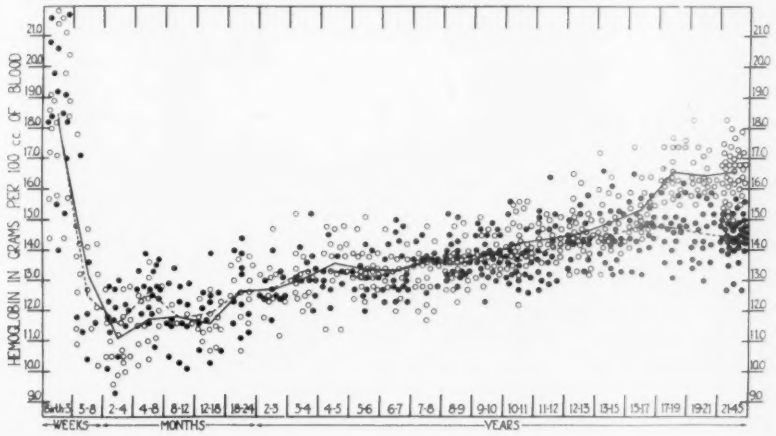
7. Heller, V. G., and Paul, H.: Changes in Cell Volume Produced by Varying Concentrations of Different Anticoagulants, J. Lab. & Clin. Med. **19**:777-780 (April) 1934.

8. Van Slyke, D. D., and Neill, J. M.: The Determination of Gases in Blood and Other Solutions by Vacuum Extraction and Manometric Measurement, J. Biol. Chem. **61**:523-573 (Sept.) 1924.

9. Wintrobe, M. M.: A Simple and Accurate Hematocrit, J. Lab. & Clin. Med. **15**:287-289 (Dec.) 1929.

RESULTS

The distribution of individual determinations of hemoglobin for the entire series of infants, children, adolescent boys, adolescent girls and adults is given in the chart. This includes data which have been reported previously,[1] together with the results of the determinations in the present study. For purposes of statistical analysis the adolescent groups are divided into four age periods of two years each. At the age of 12 years all values for both sexes are almost identical with those for the group of women. The chart shows graphically the gradual separation of averages for hemoglobin which begins in the period between 13 and 15 years. The boys reach the male adult level in the period between 17 and 19 years. The averages for the girls show only



Distribution of results of 800 determinations of hemoglobin on venous blood by the Van Slyke-Neill oxygen capacity method. The individual values are represented by open circles for 421 men and boys and by solid circles for 379 women and girls. The mean is shown by a solid line for men and boys and by a dotted line for women and girls.

a slight rise in the period between 15 and 19 years. The values for the group between 19 and 21 years are again at the adult level for women.

Table 1 gives the statistical data for the quantity of hemoglobin, the number of red blood cells and the volume of packed cells of the adolescent groups as compared with those for the adults and with those for the children 12 years of age in the previous series. The averages of the number of red blood cells and of the volume of packed cells follow the same trend as do those for the hemoglobin, and they reach the adult level at about the same age. Although the averages

TABLE 1.—*Statistical Data for Hemoglobin, Red Blood Cells and Volume of Packed Red Cells*

Number of Subjects	Age, Years	Hemoglobin						Red Blood Cells						Volume of Packed Cells					
		Mean	Standard Deviation	Probable Error of Mean	Coefficient of Variation	Actual Range		Mean	Standard Deviation	Probable Error of Mean	Coefficient of Variation	Actual Range		Mean	Standard Deviation	Probable Error of Mean	Coefficient of Variation	Actual Range	
						Minimum	Maximum					Minimum	Maximum					Minimum	Maximum
Male																			
25	12 to 13	14.53	0.89	0.12	6.1	13.2	16.5	4.67	0.23	0.03	4.8	4.34	5.10	43.04	2.09	0.28	4.8	39.0	47.7
20	13 to 15	14.90	0.95	0.14	6.4	13.2	17.2	4.81	0.32	0.05	6.6	4.34	5.41	43.70	2.98	0.45	6.8	38.1	49.0
20	15 to 17	15.30	0.73	0.11	4.7	14.1	17.4	4.98	0.31	0.05	6.2	4.28	5.60	46.10	2.14	0.32	4.6	42.7	52.8
20	17 to 19	16.57	0.64	0.10	3.8	15.5	17.7	5.35	0.22	0.03	4.1	5.02	5.78	49.55	1.87	0.28	3.7	46.7	53.3
20	19 to 21	16.45	0.62	0.09	3.7	15.5	18.3	5.35	0.28	0.04	5.3	4.80	5.90	48.70	2.19	0.33	4.5	44.4	52.5
40	21 to 45	16.54	0.81	0.09	4.8	15.0	18.3	5.42	0.25	0.03	4.6	4.83	6.07	48.35	2.17	0.23	4.4	43.8	53.6
Female																			
15	12 to 13	14.42	0.77	0.13	5.3	13.3	15.8	4.66	0.20	0.03	4.2	4.35	5.03	43.35	1.26	0.22	2.9	41.6	46.0
20	13 to 15	14.51	0.93	0.14	6.4	13.3	16.6	4.66	0.28	0.04	6.1	4.25	5.32	43.35	2.45	0.37	5.6	40.0	49.4
20	15 to 17	14.79	0.83	0.12	5.5	13.2	16.5	4.69	0.22	0.03	4.7	4.26	5.23	44.20	2.10	0.32	4.7	40.7	49.2
20	17 to 19	14.75	0.74	0.11	5.0	13.1	16.2	4.65	0.22	0.03	4.8	4.27	5.10	44.43	2.35	0.35	5.2	39.7	47.6
20	19 to 21	14.54	0.79	0.12	5.4	13.0	15.9	4.63	0.16	0.02	3.4	4.27	4.95	43.16	2.30	0.35	5.3	39.2	47.3
40	21 to 40	14.45	0.69	0.07	4.7	12.7	15.7	4.63	0.15	0.02	3.3	4.41	5.00	43.22	1.80	0.19	4.1	37.1	46.1

for hemoglobin are somewhat higher than those reported by Osgood,[4] the age for the first definite sex differences is approximately the same as that which he reported. In Williamson's group [2] the divergence in values began about two years later.

The greatest deviation of individual values from the mean appears in both sexes between the ages of 13 and 15. This variability is easily seen in the chart. Some of the hemoglobin values for boys are still in the lower portion of the range, while those for a few of the girls are similarly scattered in the upper portion. Among the values for girls are some greater than any which appear in the blood of women. It is possible that during adolescence the blood values of certain girls may undergo a temporary increase similar to the permanent rise in values for young men. Definite knowledge of such changes can be obtained only by studies of the blood of individual girls repeated at intervals through the period of their adolescent growth and development.

Table 2 gives the statistical data for the corpuscular constants in the 12 year old, adolescent and adult groups. Our previous investigations [1a, b] have shown that after the age of 3 years averages for children approximate those for adults. No definite sex differences have been observed in the size of corpuscles during childhood. In the adolescents, however, as in the adults, the mean corpuscular volume of the red blood cells is slightly less in the male than in the female. Averages for both sexes are slightly greater during adolescence than in adult life.

Osgood's series [4] differs from ours in some of the values for individual corpuscles. He found that the cells of the children were smaller and contained less hemoglobin that those of the adults of his series. The hemoglobin content of the red blood cells increased at 14 years, but the cells remained small until the subjects reached the age of 17 years. At this time he observed sex differences in the volume of the individual red blood cells similar to those which we found. Osgood described an increased hemoglobin concentration in the red blood cells of boys 14 to 19 and in girls 14 to 17 years of age. Table 2 shows that in our series the concentration of hemoglobin remains at the same uniform level during adolescence as in other age periods.

SUMMARY AND CONCLUSIONS

The quantity of hemoglobin, the number of red blood cells and the volume of packed cells were determined accurately on samples of venous blood from 80 boys and 80 girls between the ages of 13 and 21 years. The values obtained are compared with a series of 640 similar deter-

TABLE 2.—*Statistical Data for Mean Corpuscular Hemoglobin, Mean Corpusular Volume and Mean Corpuscular Hemoglobin Concentration*

Number of Subjects	Age, Years	Mean Corpuscular Hemoglobin						Mean Corpuscular Volume						Mean Corpuscular Hemoglobin Concentration					
		Mean	Standard Deviation	Probable Error of Mean	Coefficient of Variation	Actual Range		Mean	Standard Deviation	Probable Error of Mean	Coefficient of Variation	Actual Range		Mean	Standard Deviation	Probable Error of Mean	Coefficient of Variation	Actual Range	
						Minimum	Maximum					Minimum	Maximum					Minimum	Maximum
Male																			
25	12 to 13	31.1	1.67	0.23	5.3	27.5	34.3	92.1	4.47	0.60	4.8	81.2	100.5	33.7	0.77	0.10	2.2	32.2	35.0
20	13 to 15	30.9	1.28	0.19	4.1	28.6	33.0	90.8	3.35	0.51	3.6	86.2	96.8	34.0	1.11	0.17	3.2	32.3	35.9
20	15 to 17	30.7	1.21	0.18	3.9	28.1	32.9	92.5	3.93	0.59	4.2	86.0	101.4	33.1	0.71	0.11	2.1	32.0	34.1
20	17 to 19	30.9	0.80	0.12	2.6	29.1	32.6	92.6	3.62	0.55	3.9	85.2	98.2	33.4	0.77	0.12	2.3	32.1	35.0
20	19 to 21	30.7	1.43	0.22	4.6	26.8	33.1	91.0	4.59	0.69	5.0	77.6	96.8	33.8	0.99	0.15	2.9	31.6	35.1
40	21 to 45	30.5	1.39	0.15	4.5	27.2	34.0	89.2	3.82	0.41	4.2	81.3	99.6	34.2	1.17	0.12	3.4	31.9	36.8
Female																			
15	12 to 13	30.9	1.41	0.25	4.5	28.3	34.0	93.0	3.61	0.63	3.8	86.0	97.8	33.2	1.22	0.21	3.6	31.3	35.4
20	13 to 15	31.1	1.60	0.24	5.1	28.4	34.1	93.0	4.73	0.73	5.0	82.3	102.4	33.5	0.77	0.12	2.3	31.8	35.1
20	15 to 17	31.7	1.44	0.22	4.5	28.3	33.1	94.2	3.69	0.56	3.9	85.0	100.6	33.4	0.89	0.13	2.6	31.7	35.1
20	17 to 19	31.7	0.95	0.14	3.0	29.7	33.5	95.5	2.12	0.32	2.2	92.5	99.3	33.2	0.81	0.12	2.4	31.6	34.5
20	19 to 21	31.4	1.55	0.23	4.9	27.6	33.8	93.2	3.22	0.48	3.5	86.6	100.0	33.6	1.05	0.16	3.1	31.7	35.2
40	21 to 40	31.2	1.53	0.16	4.8	27.1	33.9	93.3	3.75	0.40	4.0	79.4	99.5	33.4	1.08	0.11	3.2	30.9	35.5

minations on the blood of infants, children and adults. From the results of the study, the following conclusions may be drawn:

1. Averages for boys are almost identical with those for girls at 13 years. These gradually increase to the adult level for men at 17 years. Averages for girls show little variation from the level for women during the adolescent period.

2. In the adolescent as well as in the adult, the average volume of the individual red blood cell of the male is smaller than that of the female. Values for adolescents of both sexes are slightly higher than those for adults.

3. The corpuscular hemoglobin concentration remains at the same level throughout adolescence as in other age periods.

VITAMIN C IN HUMAN PREGNANCY AND LACTATION

I. STUDIES DURING PREGNANCY

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There is evidence from animal experiments that the requirements for certain of the vitamins are increased by pregnancy. However, there is little precise information with respect to changes during pregnancy and lactation in women's needs for vitamins. The recent development of reliable methods for determining the amount of vitamin C in tissues and in biologic fluids has offered opportunity for studies during human pregnancy and lactation. A number of observations have appeared in the literature of the past three years concerning the ascorbic acid content of maternal blood, of fetal blood and of the placenta, although no one seems to have followed a series of pregnant women consistently through pregnancy and delivery to obtain related and comparative values.

Neuweiler,[1] using Gabbe's technic with modifications, reported a higher content of ascorbic acid in blood from the umbilical vein than in that from the umbilical artery (1.9 to 3.6 versus 0.7 to 2.1 mg. per hundred cubic centimeters). On the basis of this observation and of earlier work in which he found a considerable amount of ascorbic acid in the placenta, Neuweiler [2] could not accept the claim of Rohmer and Bezssonoff [3] that the human fetus can synthesize ascorbic acid. Abt, Farmer and Epstein,[4] using indophenol blue titration of a tungstic acid filtrate, reported identical values for the reduced ascorbic acid of

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1. Neuweiler, W.: Versuche über den Vitamin C Stoffwechsel beim Fetus, Klin. Wchnschr. **14**:1040, 1935.

2. Neuweiler, W.: Ueber den Gehalt der Plazenta an Vitamin C, Schweiz. med. Wchnschr. **16**:539, 1935.

3. Rohmer, P., and Bezssonoff, N.: Investigations into the Pathogenesis of Scorbutic Dystrophy, Arch. Dis. Childhood **10**:139, 1935.

4. Abt, A. F.; Farmer, C. J., and Epstein, I. M.: Normal Cevitamic (Ascorbic) Acid Determinations in Blood Plasma and Their Relationship to Capillary Resistance, J. Pediat. **8**:1, 1936.

maternal and cord blood. They concluded that there is a complete diffusion of ascorbic acid from maternal to fetal blood and that the amount in the fetal blood is dependent on the content of vitamin C in the maternal diet. Braestrup,[5] using the methylene blue technic of Lund and Lieck[6] on blood serum, has recently reported comparative values for maternal and cord blood. His average value for the content of ascorbic acid in maternal blood at delivery was 0.36 mg. per hundred cubic centimeters, while for babies under 3,000 Gm., the average value for cord blood was 1.03 mg. and for babies over 3,000 Gm., it was 0.85 mg. per hundred cubic centimeters. He states that the values for ascorbic acid for serum of women in labor are low. Braestrup also found that there was a correlation between the amounts of ascorbic acid in the maternal and the cord blood.

Wahren and Rundqvist,[7] also using the method of methylene blue reduction measured photometrically, have reported comparative values for ascorbic acid in maternal and fetal blood. The averages for 17 cases were 0.158 and 0.347 mg. per hundred cubic centimeters, respectively. The maximum values for maternal and cord blood in their series were only 0.28 and 0.48 mg. per hundred cubic centimeters, respectively. However, no statement concerning the maternal diet is included in their article, so that it is impossible to estimate whether the unusually low values reported are due to maternal diets low in vitamin C or to their method.

In this study we shall present related observations on (1) the dietary intake of vitamin C during human pregnancy, (2) the amount of ascorbic acid in the blood plasma at various stages of pregnancy, (3) the amounts of ascorbic acid in maternal plasma and in umbilical cord plasma at the time of birth and (4) the amount of ascorbic acid in the plasma of patients with hyperemesis gravidarum and with eclampsia.

METHODS OF THE PRESENT STUDY

The dietary histories of mothers and babies selected from the prenatal clinic and from the wards of the Boston Lying-in Hospital were taken and evaluated independently by one of us. Many of the patients on whom we have dietary information were selected from a special study group and were followed from early pregnancy. Histories of nutrition in this special group were taken at intervals of from three to six weeks during pregnancy, and were supplemented by periodic

5. Braestrup, P. W.: Studies of Latent Scurvy in Infants: II. Content of Ascorbic (Cevitamic) Acid in the Blood Serum of Women in Labor and of Children at Birth, Acta pædiat. **19**:328, 1937.

6. Lund, H., and Lieck, H.: Quantitative Determination of Cevitamic Acid in Blood Serum, Hospitalstid. **79**:798, 1936.

7. Wahren, H., and Rundqvist, O.: Ueber den Ascorbinsaüregehalt des Blutes von Mutter und Frucht, Klin. Wchnschr. **16**:1498, 1937.

daily records of total food intake kept by the patients. In this study group every effort was made to have the mothers improve their diet during pregnancy, so that a large percentage of the mothers undoubtedly had higher intakes of vitamin C in the later months of pregnancy. Single dietary histories were also taken of patients selected at random from the general prenatal clinic or at the time of delivery. The diets of these patients had not been influenced with respect to vitamin C during the course of pregnancy.

The ascorbic acid content of the blood plasma was estimated by titration with 2,6-dichlorophenolindophenol of a metaphosphoric acid plasma filtrate from oxalated blood to which potassium cyanide had been added, as described by Pijoan and Klemperer [8] and by Ingalls.[9]

With this technic, optimal values for ascorbic acid in the plasma of nonpregnant subjects vary from approximately 0.7 to 1.5 mg. per hundred cubic centimeters. It is thought by a number of workers that amounts below 0.6 mg. are suboptimal. Many subjects with values below 0.4 mg. do not present clinical signs of scurvy. However, suggestive changes which respond to vitamin C therapy are not uncommonly seen in the gums of patients with values for ascorbic acid in the blood plasma between 0.4 and 0.15 mg. Among 15 infants with definite clinical and roentgenographic signs of scurvy, the plasma levels of ascorbic acid as determined by Ingalls [9] ranged from 0.00 to 0.16 mg., with an average value of 0.07 mg.

There is increasing evidence that except when the values are very high or very low the level of ascorbic acid in the blood plasma is a reliable index of vitamin C nutrition. Baumann [10] has shown that the amount of ascorbic acid which may be fed without undue excretion in the urine is inversely proportional to the amount in the blood. With amounts greater than 1 mg. in the plasma, the organism is at or near saturation, and excesses of vitamin C in the diet tend to be excreted in the urine. On the other hand, very low plasma values, although they indicate definite suboptimal or deficient vitamin C nutrition, do not indicate to what extent the reserves in the tissues have been depleted.

CLINICAL OBSERVATIONS

General Correlation Between the Vitamin C Content of the Maternal Diet and the Ascorbic Acid Content of the Blood Plasma During Pregnancy.—In 99 instances appraisal of the dietary intake of vitamin C

8. Pijoan, M., and Klemperer, F.: Determination of Blood Ascorbic Acid, J. Clin. Investigation **16**:443, 1937.

9. Ingalls, T. H.: Studies on the Urinary Excretion and Blood Concentration of Ascorbic Acid in Infantile Scurvy, J. Pediat. **10**:577, 1937.

10. Baumann, T.: Die Bestimmung der physiologischen Spanne der C Vitamin Sättigung des Organismus, Klin. Wchnschr. **16**:1246, 1937.

during various stages of pregnancy was compared with the amount of ascorbic acid in the plasma. The figures in table 1 show good correlation between our independent ratings of the vitamin C content of the maternal diets and the average values for ascorbic acid in the plasma. In table 1, group A is made up of studies on 25 patients from our special study group, whose diets were influenced for the better during pregnancy, as is well illustrated by the disproportionately large number of ratings falling into the classification "normal or above." Group B in table 1, in contrast, consists of 18 patients whose diets were uninfluenced during pregnancy. In the latter group more than half of the dietary histories were classified as deficient with respect to vitamin C. Justification for our poor ratings of the maternal diets in the latter group was found in the low values for ascorbic acid in their blood.

TABLE 1.—*General Correlation Between the Maternal Intake of Vitamin C and the Average Values for Ascorbic Acid in Plasma During Pregnancy*

	No. of Dietary Histories	Rating of Maternal* Vitamin C Intake	Plasma Ascorbic Acid, Mg. per 100 Cc.	
			Mean	Sigma
Group A	43	Normal or above	0.86	0.24
	21	Suboptimal or borderline	0.54	0.26
	17	Deficient	0.25	0.14
Group B	3	Normal or above	0.97	....
	5	Suboptimal or borderline	0.61	....
	10	Deficient	0.22	0.18

* The daily intake of vitamin C was arbitrarily regarded as "normal or above" if it was estimated to contain 50 mg. of ascorbic acid (approximately the content of two oranges) or more. The term "deficient" connotes less than half the "normal" amount.

Changes in the Ascorbic Acid Content of Maternal Plasma as Pregnancy Advances.—The amount of ascorbic acid in the maternal plasma tends to decrease as pregnancy advances, as is indicated in table 2. This trend of the average values to become lower as pregnancy advances is definite, in spite of the fact that the diets of a number of the patients included in the study were improved as pregnancy advanced.

The values for ascorbic acid in the plasma in early and in late pregnancy are correlated with the estimated dietary intakes of vitamin C in table 3. It will be seen that with like dietary ratings for vitamin C the average values for ascorbic acid in the plasma are lower in the later part of pregnancy whether the vitamin C intake is optimal, suboptimal or deficient.

The downward trend of the ascorbic acid in the plasma is not inevitable. If the level is low at the onset of pregnancy, correction of the diet usually results in higher values as pregnancy advances. However, among patients in whom the ascorbic acid in the plasma was above 1 mg. per hundred cubic centimeters at the beginning of preg-

nancy (an optimum value), we have found it possible in only 3 to maintain the initial level without dietary supplement of ascorbic acid. In 1 patient the diet was supplemented with from 150 to 200 mg. of ascorbic acid daily during the last two weeks of pregnancy. The ascorbic acid in the plasma at the time of delivery was 1.6 mg. per hundred cubic centimeters. Another patient took 125 mg. of ascorbic acid daily during the last two weeks of pregnancy, in addition to an optimum diet. The ascorbic acid in the plasma at the time of delivery was only 1.0 mg. We have the definite impression that the level of ascorbic acid in the plasma does not respond so promptly to a dietary

TABLE 2.—*Average Values for Ascorbic Acid in the Plasma of 67 Patients at Various Stages of Pregnancy and at Delivery*

	Through 28th Week of Pregnancy	29th Week to Term	At Delivery
Number of determinations	51	70	55
Average value in mg. per 100 cc.	0.72	0.59	0.47
Standard deviation	0.37	0.32	0.26

TABLE 3.—*Correlation of Maternal Intake of Vitamin C with Average Values for Ascorbic Acid in Plasma in Early and Late Pregnancy*

No. of Dietary Histories	Period of Pregnancy	Rating of Vitamin C Intake	Plasma Ascorbic Acid, Mg. per 100 Cc.	
			Mean	Sigma
21	First 28 weeks	Normal or above	1.04	0.26
25	29th-40th week	Normal or above	0.89	0.18
13	First 28 weeks	Suboptimal	0.66	0.21
13	29th-40th week	Suboptimal	0.45	0.22
11	First 28 weeks	Deficient	0.29	0.19
14	29th-40th week	Deficient	0.19	0.12

supplement of ascorbic acid during late pregnancy as it does in the nonpregnant state.

Relation Between the Ascorbic Acid Content of Plasma from Maternal Blood at the Time of Delivery and That of Plasma from the Umbilical Cord Blood of the Newborn.—In 31 instances comparison was made between the amounts of ascorbic acid in maternal and cord blood plasma at the time of birth. In each instance the amount was materially greater in the sample of cord blood. The average value for the 31 maternal specimens was 0.52 mg. per hundred cubic centimeters, whereas that for the 31 infants was 1.28 mg. In 24 of these cases, the dietary history of the mother was obtained. The values for ascorbic acid in maternal and in cord blood are correlated with the dietary histories in table 4. It is of interest that, in general, the higher

the level of ascorbic acid in maternal plasma, the less the difference between the value in the maternal and that in the cord blood. On the other hand, in those instances in which both the maternal dietary history and the amount of ascorbic acid in the maternal plasma indicated marked deficiencies, the values found for cord plasma at birth were three, four or more times as great. Although there were 6 instances in which the maternal plasma contained 0.2 mg. of ascorbic acid or less per hundred cubic centimeters (values which are often found associated with clinical scurvy), in no instance was the amount in the cord plasma less than 0.5 mg.

In 7 instances the ascorbic acid was determined in plasma from the umbilical artery and vein. In each case the value was slightly higher

TABLE 4.—*Ascorbic Acid Content of Plasma of Maternal and Cord Blood Taken at the Time of Delivery*

Vitamin C Content of Maternal Diet					
Normal or Above		Suboptimal		Deficient	
Plasma Ascorbic Acid, Mg. per 100 Cc.		Plasma Ascorbic Acid, Mg. per 100 Cc.		Plasma Ascorbic Acid, Mg. per 100 Cc.	
Maternal Blood	Cord Blood	Maternal Blood	Cord Blood	Maternal Blood	Cord Blood
1.0	1.9	0.5	1.8	0.1	0.5
0.8	1.5	0.1	0.5	0.2	0.6
0.6	1.4	0.4	1.5	0.1	1.0
1.0	1.9	0.5	1.0	0.1	0.8
0.9	1.7	0.5	1.0	0.2	1.0
0.9	2.4	0.6	1.3	0.5	1.2
0.8	1.7	0.5	1.4	0.5	1.1
1.0	1.7	0.4	1.0	...	...
1.0	1.8	...	...	...	...
Average Values in Mg. per 100 Cc.					
0.88	1.77	0.44	1.19	0.24	0.89

in blood from the umbilical vein (blood coming *from* the placenta) than in that from the umbilical artery. The average values were respectively 0.80 and 0.75 mg. per hundred cubic centimeters.

Values for Ascorbic Acid in the Plasma of Patients with Hyperemesis and Eclampsia.—The amount of ascorbic acid in the plasma of 3 patients with severe and prolonged hyperemesis gravidarum was determined. In 2 instances there was less than 0.1 mg. per hundred cubic centimeters, and in the other the value was 0.2 mg. One of the patients had clinical scurvy, which responded promptly to vitamin C therapy. The condition of the gums improved with therapy in the other 2 patients. These observations confirm for vitamin C the impression that vitamin deficiencies may come to play important roles in the pathology of prolonged hyperemesis. Blood was taken for analysis from 3 patients with eclampsia. The respective values for ascorbic acid were 0.5, 0.5 and 1.1 mg. per hundred cubic centimeters.

COMMENT

These studies show good correlation between the vitamin C content of the maternal diet and the amount of ascorbic acid in the maternal plasma. They also indicate that with a relatively constant intake of vitamin C the amount of ascorbic acid in maternal blood plasma decreases markedly as pregnancy advances. This seems to be true whether the dietary intake of vitamin C is optimal, suboptimal or deficient. The average amount of ascorbic acid in maternal plasma at the time of delivery was only a little more than half that present during the first twenty-eight weeks of pregnancy (0.43 and 0.72 mg. per hundred cubic centimeters, respectively).

SUMMARY AND CONCLUSION

The amount of ascorbic acid in plasma from the cord blood of infants at birth is from two to four or more times greater than that in maternal plasma taken at the time of delivery. The greatest differences are found when the values for the maternal blood are lowest. Plasma from the umbilical vein contains slightly more ascorbic acid than that from the umbilical artery.

In 3 cases of hyperemesis gravidarum the ascorbic acid in the plasma was within the range found in cases of clinical scurvy. The ascorbic acid in the plasma in 3 cases of eclampsia was within normal range.

In conclusion, we believe that these studies justify the following statements:

1. The maternal need for vitamin C is considerably increased during pregnancy. The diets of the women in our clinic were in most instances not adequate to meet this increased need. The inadequate intakes of vitamin C found in the maternal diets were confirmed by suboptimal values for ascorbic acid in plasma.

2. The fetus in utero acts parasitically on the mother with respect to vitamin C. So long as appreciable amounts of ascorbic acid are present in maternal plasma, the fetus tends to take what it needs irrespective of the maternal requirements.

3. Patients with prolonged hyperemesis gravidarum may acquire severe vitamin C deficiency.

VITAMIN C IN HUMAN PREGNANCY AND LACTATION

II. STUDIES DURING LACTATION

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In the preceding communication,[1] it has been shown that the fetus acts as a parasite on the mother for its vitamin C and that the requirement of the mother for this substance is therefore considerably increased during pregnancy. In this paper, we shall present data on the vitamin C content of breast milk and of maternal and infant blood plasma during the nursing period.

In 1936, several investigators reported on the vitamin C content of human milk. Kasahara and Kawashima's [2] values were between 4.2 and 5.6 mg. per hundred cubic centimeters, and Wachholder's [3] averaged 4.4 mg. Stoerr [4] reported an average of 3 mg. and found the figure slightly higher for colostrum. De Haas and Meulemans [5] found the colostrum of native Indian and Chinese women to contain 5 mg. of ascorbic acid per hundred cubic centimeters, while milk sampled later in the puerperium contained about 4 mg.; they estimated that a breast-fed infant obtained approximately 40 mg. of ascorbic acid daily.

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From the Harvard School of Public Health, the Boston Lying-in Hospital and the Children's Medical Service of the Massachusetts General Hospital.

1. Teel, H. M.; Burke, B. S., and Draper, R.: Vitamin C in Human Pregnancy and Lactation: I. Studies During Pregnancy, Am. J. Dis. Child., this issue, p. 1004.

2. Kasahara, M., and Kawashima, K.: Die jahreszeitliche Schwankung des Vitamin C-Gehaltes in der Muttermilch, Ztschr. f. Kinderh. **58**:191-192, 1936.

3. Wachholder, K.: Die Versorgung des Säuglings mit Vitamin C, Klin. Wchnschr. **15**:593-596 (April 25) 1936.

4. Stoerr, E.: Le lait en tant que source de vitamine C (lait de femme, lait de vache cru et chauffé, ses variations saisonnières, lait condensé et lait sec), Rev. franç. de pédiat. **12**:427-438, 1936.

5. de Haas, J. H., and Meulemans, O.: Ascrobic Acid (Vitamin C) Content of Mother's Milk at Batavia, Indian J. Pediat. **3**:216-233 (Oct.) 1936.

Selleg and King [6] found the vitamin C content of human milk to vary from 1.2 to 10.8 mg. per hundred cubic centimeters, the average in 53 cases, three to six days post partum, being 5.5 mg. When the women were on a good hospital diet without special supplements, the average value rose gradually to 6.4 mg. on the tenth day. The values for two groups receiving orange juice supplements equivalent to 210 and 430 mg. of vitamin C per day rose to 7.3 and 8.1 mg. per hundred cubic centimeters, respectively, on the tenth day. These authors estimated that the breast-fed infant obtained from 40 to 50 mg. of ascorbic acid a day during the first few weeks of life.

In the present investigation we have undertaken further studies and have correlated our data with the ascorbic acid content of the plasma of mother and infant.

METHODS

The ascorbic acid content of the blood plasma was determined with 2, 6-dichlorophenolindophenol, as described by Pijoan and Klemperer [7] and by Ingalls.[8]

We have devised the following method for determining the ascorbic acid content of human milk, using metaphosphoric acid for precipitation of protein, as advocated for blood assay by Fujita and Iwatake.[9]

Five cubic centimeters of whole milk is preserved with 1 drop of a 1 per cent solution of potassium cyanide. Two cubic centimeters of a 10 per cent solution of metaphosphoric acid and 3 cubic centimeters of distilled water are added, and the mixture is well stirred. The curd thus precipitated is filtered through a pleated Whatman no. 44 filter paper. Two cubic centimeters of the filtrate is then titrated with a 0.01 per cent solution of 2, 6-dichlorophenolindophenol. A blank, using distilled water instead of milk, must be subtracted from the titration figure.

HOSPITAL DIET

Our first series of observations was made on a group of 17 mothers in the wards of the Boston Lying-in Hospital. They received the regular hospital diet, the ascorbic acid content of which was calculated from the diet tables of Rose [10] and found not to exceed 20 mg. of ascorbic acid a day (table 1).

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6. Selleg, I., and King, C. G.: The Vitamin C Content of Human Milk and Its Variation with Diet, J. Nutrition **11**:599-606 (June) 1936.

7. Pijoan, M., and Klemperer, F.: Determination of Blood Ascorbic Acid, J. Clin. Investigation **16**:443 (May) 1937.

8. Ingalls, T. H.: Studies on the Urinary Excretion and Blood Concentration of Ascorbic Acid in Infantile Scurvy, J. Pediat. **10**:577-591 (May) 1937.

9. Fujita, A., and Iwatake, D.: Ueber die Bestimmung von Vitamin C mittels 2, 6-Dichlorphenol-indophenol, Biochem. Ztschr. **277**:293-295, 1935.

10. Rose, M. S.: A Laboratory Handbook for Dietetics, New York, The Macmillan Company, 1937.

The average vitamin C content of the plasma on the first day post partum was 0.34 mg. per hundred cubic centimeters. Values of 0.5 mg. or higher are generally accepted as normal and of 0.3 mg. or lower as indicating a definitely deficient intake of ascorbic acid.[11] The low figures obtained in this study may be due in part to a diminished food intake for the previous thirty-six hours, but it is probable that in a majority of the patients the diet previous to delivery had been inadequate to maintain the normal ascorbic acid content of the blood.

The ascorbic acid content of the blood plasma one week and two weeks post partum was nearly the same as one day post partum (average, 0.30 mg. per hundred cubic centimeters). The amount in the breast

TABLE 1.—*Ascorbic Acid Concentration During the First Two Weeks of the Puerperium in the Blood and in the Breast Milk of Seventeen Mothers on the Usual Hospital Diet*

Days post partum	1	4-5	7	7-8	14	14
	Blood, Mg. per 100 Cc.	Milk, Mg. per 100 Cc.	Blood, Mg. per 100 Cc.	Milk, Mg. per 100 Cc.	Blood, Mg. per 100 Cc.	Milk, Mg. per 100 Cc.
J. E.	0.2	...	0.2	3.5	0.2	2.6
H. M.	0.7	4.3	0.6	4.0	0.3	5.4
C. H.	0.1	2.0	0.3	2.7	0.2	2.8
M. H.	0.3	5.0	0.3	4.9	0.2	4.5
E. F.	0.6	2.9	0.4	Breasts dried up		
M. H.	0.2	3.9	0.3	4.5	...	4.6
M. S.	0.5	5.9	0.3	5.7	...	5.2
M. E.	0.3	4.9	0.3	4.9	0.4	4.7
M. M.	0.3	7.2	0.4	5.9	0.4	5.8
H. D.	0.5	4.6	0.3	6.6	0.4	6.1
L. O.	0.3	4.5	0.2	4.8	0.3	4.8
M. S.	0.2	3.7	0.3	6.0	Breasts dried up	
A. W.	0.2	3.2	0.2	3.9	0.3	5.0
J. M.	0.3	3.6	0.2	3.5	...	3.8
T. F.	0.5	4.8	0.2	4.1	...	5.2
H. M.	0.4	4.0	0.4	3.5	Breasts dried up	
C. O.	0.1	1.7	0.2	Breasts dried up		
Average	0.34	4.39	0.30	4.57	0.30	4.65

milk varied between 1.7 and 7.2 mg. per hundred cubic centimeters, and for the individual mother the percentages of ascorbic acid on the fourth, seventh and fourteenth days post partum were approximately the same.

Assuming that during the second week the babies of these mothers nursed an average of 3½ ounces (99 cc.) six times a day, the daily ration contained 28 mg. of ascorbic acid. This 28 mg. obtained by the infants is in excess of the 20 mg. a day received by the mothers.

The concentration of ascorbic acid in the milk was from six to twenty times higher than that in the plasma. This indicates that the

11. Abt, A. F.; Farmer, C. J., and Epstein, I. M.: Normal Cevitamic (Ascorbic) Acid Determinations in Blood Plasma and Their Relationship to Capillary Resistance, J. Pediat. **8**:1-19 (Jan.) 1936. Chu, F., and Sung, C.: The Vitamin C Content of the Blood Plasma in Normal and Sick Children, Chinese M. J. **52**:791-806 (Dec.) 1937. Pijoan and Klemperer.[7] Ingalls.[8]

presence of ascorbic acid in human milk is due to a secretory process and not to simple diffusion.

HIGH VITAMIN C DIET

The second group of observations was on 19 mothers who received, in addition to the regular ward diet, daily supplements of 300 or 600 mg. of ascorbic acid in divided doses, beginning on the first day of the puerperium (table 2). Several of these mothers had slightly higher initial levels of ascorbic acid in the plasma; therefore, the average on the first postpartum day was 0.1 mg. per hundred cubic centimeters

TABLE 2.—*Ascorbic Acid Concentration During the First Two Weeks of the Puerperium in the Blood and Milk of Nineteen Mothers Given the Usual Hospital Diet Plus 600 or 300 Mg. of Ascorbic Acid Daily*

Days post partum	1	4-5	7	7-8	14	14	
	Blood, Mg. per 100 Cc.	Milk, Mg. per 100 Cc.	Blood, Mg. per 100 Cc.	Milk, Mg. per 100 Cc.	Blood, Mg. per 100 Cc.	Milk, Mg. per 100 Cc.	Daily Dose Vitamin C, Mg.
C. F.	0.2	...	1.4	8.4	1.4	8.2	600
C. E.	0.6	6.4	1.1	6.4	1.6	5.0	600
M. Y.	0.4	5.2	0.8	4.5	...	7.6	600
H. W.	0.2	...	1.9	7.7	...	9.2	600
L. E.	0.3	...	1.4	7.5	1.3	...	600
R. L.	0.8	6.7	1.7	6.2	...	7.1	600
T. D.	1.0	7.5	1.7	5.1	2.0	8.0	300
E. P.	0.5	6.4	1.0	Breasts dried up			300
E. R.	0.6	6.2	0.9	9.5	...	...	300
M. M.	0.5	6.4	1.0	8.0	...	...	300
M. S.	0.4	6.9	1.2	7.2	...	...	300
M. H.	0.7	...	1.4	7.5	...	...	300
E. S.	0.5	5.4	1.7	7.0	...	7.1	300
M. B.	0.2	4.0	1.8	7.3	...	7.3	300
E. M.	0.3	6.1	1.5	6.5	1.5	7.1	300
D. J.	0.2	...	1.5	6.6	...	7.7	300
V. J.	0.4	9.1	1.4	7.9	1.2	...	300
M. G.	0.2	5.6	1.5	...	1.2	6.9	300
H. T.	0.6	8.6	1.3	9.1	1.3 Breasts dried up		300
Average	0.45	6.46	1.38	7.20	1.44	7.38	

higher than that for the preceding group. The ascorbic acid of the blood one week and two weeks post partum rose to 1.38 and 1.44 mg. per hundred cubic centimeters—more than four times the figure for the control group. The ascorbic acid content of the milk averaged 7.20 and 7.38 mg. per hundred cubic centimeters, as contrasted with 4.57 and 4.65 mg. in the control group, an amount greater by 60 per cent. We have estimated that the breast-fed babies of this group, receiving 3½ ounces (99 cc.) of milk every four hours, obtained 44 mg. of ascorbic acid per day.

The mothers receiving the 300 mg. supplement showed as high a concentration of ascorbic acid in the blood and in the milk as those mothers receiving the 600 mg. supplement. This indicates that in both groups the saturation level of ascorbic acid in the plasma had been reached by the end of the first week, the excess of vitamin probably being excreted in the urine.

MASSIVE DOSES OF VITAMIN C

The effect of massive doses of vitamin C on the ascorbic acid content of the breast milk and the plasma of one mother is demonstrated in table 3. The patient was given 600 mg. of ascorbic acid daily from the eighth to the twelfth day of the puerperium. On the twelfth day, the breasts were pumped dry; then 200 mg. of a sodium salt of synthetic ascorbic acid was injected intravenously. At the end of one hour, the injection was repeated.

The maximum content of ascorbic acid in the breast milk of this mother was 11.6 mg. per hundred cubic centimeters, a value only a little higher than that reported for some mothers in table 2. The ascorbic acid value in the blood plasma was 4.0 mg. per hundred cubic centimeters after the first injection. The value rapidly fell to a normal

TABLE 3.—*Effect of the Intravenous Injection of Ascorbic Acid on the Concentration of Ascorbic Acid in the Breast Milk of a Patient (M. B. Aged 19) Already Saturated with Vitamin C*

Postpartum Day	Ascorbic Acid		
	Intake, Mg.	Plasma Content, Mg. per 100 Cc.	Milk Content, Mg. per 100 Cc.
First to eighth	20 daily, orally	0.4	6.5
Eighth to twelfth	600 daily, orally	...	...
Twelfth			
9:00 a.m.	.....	1.1	10.0
9:09 a.m.	200 intravenously		
9:11 a.m.	.....	4.0	....
10:10 a.m.	.....	1.4	....
10:11 a.m.	200 intravenously		
10:13 a.m.	.....	4.2	....
10:15 a.m.	.....	...	11.6
11:05 a.m.	.....	...	10.1

level. The disappearance of ascorbic acid from the plasma is probably accompanied by the excretion into the urine of the greater portion of the ascorbic acid injected.[12]

VITAMIN C IN INFANT PLASMA

The effect of the vitamin C content of the mother's diet on the ascorbic acid content of the infant's blood plasma is shown in table 4. There was 1.4 mg. of ascorbic acid per hundred cubic centimeters of plasma of infants nursed by the mothers who received 300 mg. in addition to the 20 mg. of the usual hospital diet. This amount is the same as that in the blood plasma of their mothers (table 2). The ascorbic acid content of the plasma of infants whose mothers were on the usual hospital diet was 0.87 mg. per hundred cubic centimeters, a figure which is more than twice that found for their mothers at the same time

12. Johnson, S. W., and Zilva, S. S.: Urinary Excretion of Ascorbic and Dehydroascorbic Acids in Man, Biochem. J. **28**:1393-1408, 1934.

(0.30 mg.). In both instances the amount of ascorbic acid in the plasma was much higher than that found in infants on a pasteurized cow's milk formula without vitamin C supplement. The fact that mothers on a diet relatively low in vitamin C will secrete in the milk amounts of ascorbic acid so large that the ascorbic acid content of the infant's plasma is higher than that of the mother's is indicative of an interesting biologic mechanism whereby the child receives the vitamin at the expense of its mother.

TABLE 4.—*Ascorbic Acid in the Plasma of Babies on the 13th and 14th Days of Life: Group I, Breast-Fed Babies of Mothers Receiving 300 Mg. Ascorbic Acid as a Daily Supplement to the Diet; Group II, Breast-Fed Babies of Mothers on Usual Hospital Diet; Group III, Babies Fed on Pasteurized Cow's Milk Formula*

Plasma Ascorbic Acid, Mg. per 100 Cc.					
Group I		Group II		Group III	
1.1	1.5	0.6	0.9	0.2	0.4
1.4	1.6	0.7	1.0	0.2	0.4
1.4		0.9	1.1	0.2	0.4
Average 1.4		Average 0.87		Average 0.3	

TABLE 5.—*Ascorbic Acid Concentration in Breast Milk Sampled After the First Month of the Puerperium. All Subjects Nursed Their Babies and Sold Excess Milk to the Directory for Mother's Milk*

Subject	Month of Puerperium	Ascorbic Acid in Milk, Mg. per 100 Cc.	Excess, Oz. of Milk*
A. R.	1	2.5	40
E. M.	1	2.6	14
S. C.	1½	4.9	6
B. B.	2	3.2	20
L. M.	2½	3.0	40
K. W.	3	3.4	31
I. Y.	5	2.1	32
A. L.	6	5.9	8
K. M.	8	4.4	12
Average		3.38	

* All these quantities are excess milk after nursing the infant.

BREAST MILK LATER IN THE PUERPERIUM

Data on the ascorbic acid content of the milk at later periods in the puerperium are presented in table 5. The specimens for these observations were obtained through the Directory for Mother's Milk. Samples of breast milk were received from 9 mothers at periods from the first to the eighth month of the puerperium. In general, the milk of those mothers who produced the larger amounts of milk contained smaller concentrations of ascorbic acid than did the the milk of lesser producers.

On the basis of the amounts of ascorbic acid found in the breast milk of these women, it was calculated that their babies were receiving approximately 25 to 50 mg. of ascorbic acid daily.

BREAST MILK AFTER PASTEURIZATION

The influence of pasteurization and of delay in marketing on the vitamin C content of woman's milk is shown in table 6.

The Directory of Mothers' Milk at the Boston Lying-in Hospital dispenses pasteurized mothers' milk for babies that offer feeding difficulties. The mothers in their homes hygienically express the milk and put it on ice. Once a day a visiting nurse makes a collection and brings it to the hospital, where it is pooled and pasteurized. There is ordinarily an interval of twenty-four to forty-eight hours between the

TABLE 6.—*Ascorbic Acid Content of Pooled Mother's Milk Before and After Pasteurization and Content of Doubly Pasteurized Cow's Milk.**

Pooled Mother's Milk			
Before Pasteurization, Mg. per 100 Cc.	After Pasteurization, Mg. per 100 Cc.	After Delivery, Mg. per 100 Cc.	Cow's Milk Doubly Pasteurized, Mg. per 100 Cc.
1.5	0.2	0.1	0.1
1.6	0.3	0.1	0.1
1.7	0.5	0.1	0.1
1.9	0.7	0.2	0.1
2.4	0.8	0.2	0.1
2.6	0.8	0.3	0.1
2.6	0.9	0.3	0.1
2.7	1.0	0.4	0.1
2.8	1.0	0.5	0.1
2.8	1.2	1.0	0.1
Average 2.26	0.74	0.32	0.1

* These are random samples arranged in order of magnitude. No attempt has been made here to study the rate of ascorbic acid destruction in individual specimens of milk or the factors involved.

expression of the milk and its consumption. During this time there is some oxidation of the ascorbic acid. Selleg and King [6] have noted an average loss in titration values of 27 per cent when breast milk was kept in a refrigerator for eighteen hours.

In the milk which before pasteurization contained 2.26 mg. of ascorbic acid per hundred cubic centimeters, or about half the amount found in fresh milk as shown in table 1, the content diminished to 0.74 mg. after pasteurization and to 0.32 mg. after delivery to the infants' ward of a neighboring hospital. Thus, mother's milk dispensed under these conditions provides less than a tenth of the amount of vitamin C present in fresh breast milk. If 1 liter of such milk were consumed a day, the total amount of vitamin C obtained would be approximately 3 mg. It is obvious from these data that artificial feedings of pasteurized, marketed woman's milk must be considered a

negligible source of vitamin C. It is practically as important to supplement such feedings as it is to supplement formulas of pasteurized cow's milk.

COMMENT

It has been shown in the previous paper that the fetus builds up a substantial reserve of vitamin C at the expense of the mother, so that cord plasma at birth was found to contain an average of 1.3 mg. of ascorbic acid. Such plasma levels, both in adults and in babies, are associated with a saturation of ascorbic acid. This saturation of the fetus was shown to occur even when the maternal plasma contained less than a third or a quarter of the amount of ascorbic acid found in the infant plasma.

Our data in the present study show that after birth also the breast-fed infant may obtain adequate vitamin C nutrition at the expense of the mother, even if her diet is relatively deficient as indicated by a low concentration of ascorbic acid in her plasma. Continued subsistence of the mother on a scurvy-producing diet, however, would doubtless result eventually in the occurrence of scurvy in the infant. It is of interest that the quantity of vitamin C secreted in breast milk may be 20 to 50 mg. per twenty-four hours even when the maternal diet contains no more than 20 mg. of ascorbic acid a day. This must mean that the increased maternal need for the vitamin during pregnancy extends into the nursing period as well.

SUMMARY AND CONCLUSIONS

Fresh breast milk from mothers on the usual diet of a maternity ward was found to contain an average of 4.5 mg. of ascorbic acid per hundred cubic centimeters during the first two weeks of lactation. The breast-fed babies of such mothers receive an average of 28 mg. of ascorbic acid daily.

When a liberal amount of vitamin C was added to the mother's diet, the ascorbic acid content of the breast milk increased to 7.3 mg. per hundred cubic centimeters. The babies of such mothers receive an average of 46 mg. of ascorbic acid daily.

The highest concentration of ascorbic acid we found in breast milk was 11.6 mg. This followed the giving of massive doses of the vitamin orally and intravenously.

The breast milk of mothers who sell their excess supply contained an average of 3.7 mg. of ascorbic acid; this had diminished, however, to 0.3 mg. after pasteurization and marketing. Therefore, the infant being fed pasteurized human milk receives a grossly inadequate supply of vitamin C unless he is given an additional amount of the vitamin.

Since the concentration of ascorbic acid in human milk is considerably greater than that in the blood plasma, it is apparent that ascorbic acid is secreted rather than diffused into the milk. The amount of ascorbic acid in breast milk is definitely influenced by the mother's dietary intake of ascorbic acid.

An infant may obtain adequate vitamin C at the expense of a mother whose diet is relatively deficient. The biologic mechanism which furnished the fetus with adequate vitamin C during pregnancy has a counterpart which furnishes the infant with ample vitamin C during the nursing period.

Vitamin C nutrition in nursing infants is dependent on the ascorbic acid content of the breast milk, which is in turn influenced by the vitamin C intake of the mother. The increased maternal need for vitamin C which has been demonstrated to exist during pregnancy persists during the nursing period.

OSTEOPETROSIS (MARBLE BONES)

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Since Albers-Schönberg,[1] in 1904, demonstrated diffuse osteosclerosis in the living subject by means of the roentgenogram, interest in this rare disease has grown. Although reports of 80 cases have appeared in the literature,[2] in few cases has the condition been studied completely or followed for a long period. We have been fortunate in having the opportunity to observe a patient with diffuse osteosclerosis, or osteopetrosis, since early infancy. We here present not only the clinical progress of the disease as shown by the roentgenograms but our metabolic, chemical and histologic studies.

REPORT OF A CASE

At the time of writing (March 1938) E. C. is 5½ years old. When he was 1 year of age the foster mother brought him to the outpatient department of the Children's Memorial Hospital because of his blindness. She was sure he had not been able

From the Children's Memorial Hospital, the Otho S. A. Sprague Memorial Institute and the Physiology Department of Northwestern University Medical School.

1. Albers-Schönberg, H.: (*a*) Röntgenbilder einer seltenen Knochenerkrankung, München. med. Wchnschr. **51**:365, 1904; (*b*) Eine bisher nicht beschriebene Allgemeinerkrankung des Skelettes im Röntgenbild, Fortschr. a. d. Geb. d. Röntgenstrahlen **11**:261, 1907.

2. (*a*) McCune, D. J., and Bradley, C.: Osteopetrosis (Marble Bones) in an Infant, Am. J. Dis. Child. **48**:949 (Nov.) 1934. (*b*) Ellis, R. W. B.: Osteopetrosis, Proc. Roy. Soc. Med. **27**:1563, 1934. (*c*) Shallow, T. A.; Davis, W. B., and Farrel, J. T.: Osteopetrosis, Ann. Surg. **100**:512, 1934. (*d*) Root, J. H.: Albers-Schönberg's Disease, Am. J. Dis. Child. **49**:964 (April) 1935. (*e*) Pounders, C.: Congenital Osteosclerosis (Marble Bone), Ann. Int. Med. **8**:966, 1935. (*f*) Parenti, G. C.: La malattia delle ossa di marmo; morbo di Albers-Schönberg, abstracted, Surg., Gynec. & Obst. **62**:362, 1936. (*g*) Wortis, H.: Osteopetrosis, Am. J. Dis. Child. **52**:1148 (Nov.) 1936. (*h*) Kerr, H. D.: A Case of Osteopetrosis Complicated by Osteogenic Sarcoma, Am. J. Roentgenol. **35**:212, 1936. (*i*) McPeak, C. N.: Osteopetrosis, ibid. **36**:816, 1936. (*j*) Harnapp, G. O.: Zum Bilde der Marmorknochenkrankheit: die familiäre, gutartige Form der diffusen Osteosklerose, Monatschr. f. Kinderh. **69**:1, 1937.

to see since he was 6 months old. His birth was normal. On the second day of life he began to have cyanotic attacks followed by convulsions. A roentgenogram was taken, and the diagnosis was enlargement of the thymus. Despite roentgen therapy the convulsions continued until the infant was 11 weeks old.

Because of the blindness, the eyes were examined. The diagnosis was atrophy of both optic nerves. As in some other cases of marble bones with blindness, syphilis was suspected as the cause of the optic atrophy. The patient, however, had a negative Wassermann reaction.

During the next three years the child was seen many times in the otolaryngologic clinic because of a profuse nasal discharge. Finally, in September 1936, when he was brought in because of inability to elevate the right shoulder, a roentgenogram was taken. This revealed the markedly increased density of all the bones of the shoulder girdle. Roentgenograms of the remainder of the skeleton demonstrated that the osteosclerosis was generalized. It was then learned that the boy had previously sustained three pathologic fractures of different bones. Other points of interest in his history were delay in walking, arrested dentition and parental consanguinity. He walked at 18 months and had 5 teeth at 6 months, but none had erupted since. His dietary history was good. Administration of orange juice was begun when he was 3 weeks old and of cod liver oil at 6 weeks. Both had been continued until the time of admission, Sept. 14, 1936.

Physical examination revealed a stocky white boy of 4 years who was somewhat short for his age (36 inches [91 cm.]), with a marked pigeon breast deformity and moderate bowing of the legs (fig. 1). He had a square head, a low forehead with prominent frontal bosses, and the expressionless face of one who is blind. The pupils were dilated and fixed, and there was atrophy of both optic nerves. There was a profuse purulent nasal discharge. Only 5 teeth were present, 3 upper and 2 lower incisors, and these were badly carious at the gingival margins. Hearing seemed to be somewhat impaired, and speech was indistinct. The skin was dry and excoriated in places, particularly in the antecubital fossae. There was no generalized lymphadenopathy, and the liver and spleen were not palpable. One could palpate a clublike enlargement at the distal end of each femur, humerus and tibia.

This patient has been in the hospital for observation since September 1936, except for a month's venture into a foster home. During that month he fell while walking about in the house and sustained a fracture of the right femur (fig. 5).

At the time of writing the boy has grown to 37.5 (95 cm.) inches in height but has not gained any weight. He has responded moderately well to training; so it is probable that the apparent mental retardation observed at the time of his first admission was due to lack of training.

Roentgen examination revealed a marked increase in density of all the bones of the skeleton. There was a broad flaring of the ends of the long bones, giving a dumbbell-like appearance (figs. 2, 3 and 4). The shadows of the marrow cavities were greatly reduced (figs. 3 and 4). On the long bones one also saw alternating transverse bands of greater and lesser density parallel to the epiphysial lines. These were best seen at the distal end of the femur and at the proximal end of the tibia (figs. 2 and 3). Similar bands parallel to the epiphysial lines of the iliums gave them a fanlike appearance.

The bones of the base of the skull were very dense, and there was a characteristic clublike thickening of the posterior clinoid processes (fig. 7). Encroachment on the optic foramina was well demonstrated by the small aperture indicated in

figure 9 *B*. This sclerosing process involved the alveolar arches, which presented a uniform density interrupted by only 5 deciduous teeth and a few irregularly spaced tooth buds.

At the time of writing, the recent fracture of the right femur is healing in the normal time with the formation of a callus that appears chalky white in the roentgenogram.

We were fortunate in having the early roentgenograms of the chest. The first (fig. 10) was taken when the boy was 10 days old; it was interpreted as showing an enlarged thymus. Even at this early time the bones were denser than normal. When the infant was 10 weeks old, after two roentgen treatments over the mediastinum, another roentgenogram was taken (fig. 11). In this was seen the first transverse band at the metaphysis of the proximal end of the humerus.

Fig. 1.—E. C., 5 years old. Note the expressionless face of a blind child, the pigeon breast deformity and scars marking sites of removal of material for biopsies.

These roentgenograms established proof that osteopetrosis existed so early that the process must have begun in utero.

Studies of the blood on admission gave approximately normal findings: hemoglobin content, 70 per cent (Sahli); erythrocytes, 5,430,000; leukocytes, 13,700, with 56 per cent polymorphonuclears, 35 per cent lymphocytes, 7 per cent monocytes and 2 per cent eosinophils. There were no immature forms in the peripheral blood. A sternal puncture proved unsuccessful because of the advanced calcification of the sternum. Smears of the marrow made at the time of the biopsy of the rib were normal. During the past year hypochromic anemia has developed, as shown by a hemoglobin content of 55 per cent (Sahli) and an erythrocyte count of 3,500,000. There has been slight leukocytosis practically all the time, which may be due to the frequent exacerbations of nasopharyngitis and sinusitis. The differential count has been compatible with a low grade infection.

The calcium and the phosphorus content of the serum have remained normal during the entire period of observation, including a period when desiccated thyroid and parathyroid extract were being administered. The calcium content varied from 9.1 to 10.7 mg. and the phosphorus content from 3.2 to 4.3 mg. per hundred cubic centimeters. The phosphatase content of the serum was 3 Bodansky units, somewhat low for a child.

A biopsy of the proximal metaphysis of the left tibia was done on Nov. 10, 1936, and of the costochondral junction of the sixth rib on the right, on June 5, 1937.

Figure 2

Figure 3

Fig. 2.—Pelvis and femurs. The clubbing at the ends of the long bones, the increased density and the alternating lines of greater and lesser density parallel to the epiphysis can be seen here.

Fig. 3.—Lower left extremity, showing the site of removal of the biopsy material which is represented microscopically in figure 14.

Grossly the specimen of tibia was divided into two parts: one dense and colorless, the other somewhat porous and pink. All specimens were pulverized with difficulty; they seemed to have no definite planes of cleavage, fragmenting in the irregular fashion of glass.

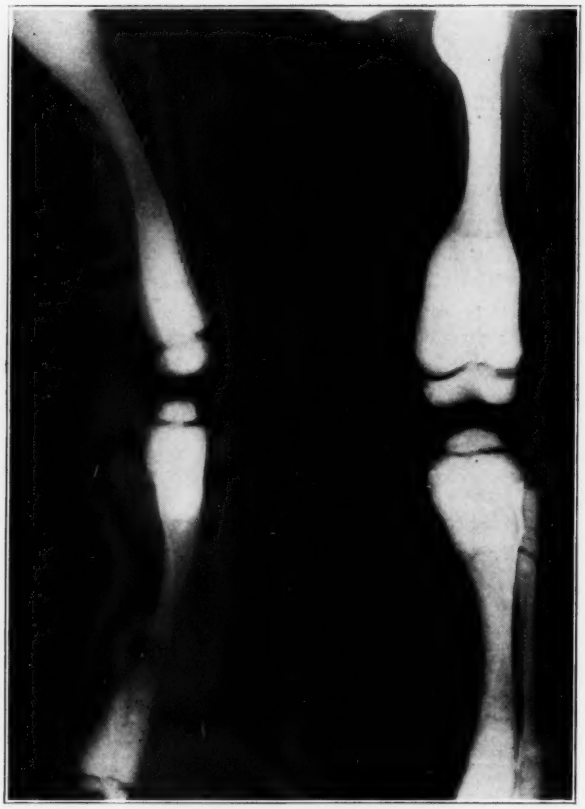

Fig. 4.—Lateral view showing the nature of the thickening at the ends of the long bones.

Fig. 5.—Right femur one month after a pathologic fracture. Note the density of the callus.

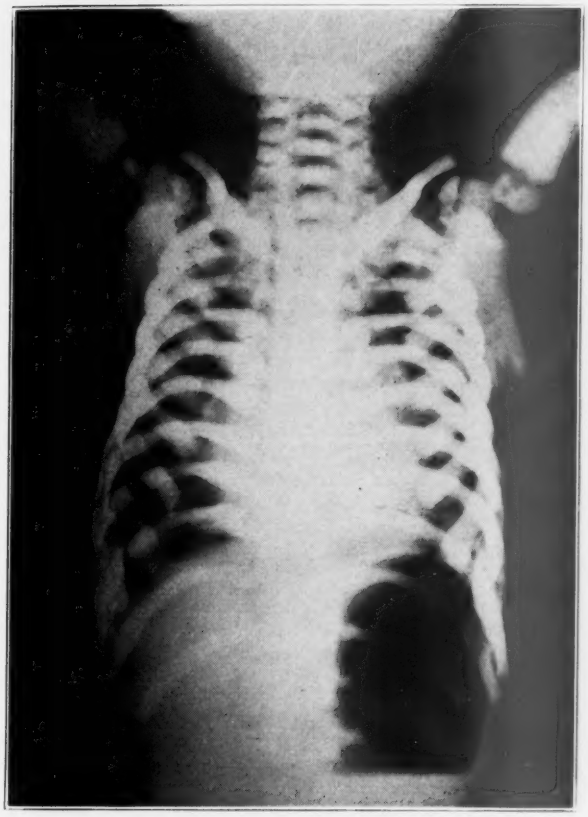

Fig. 6.—Note the density of the bones of the thoracic cage, clubbing of the proximal ends of the humeri and the transverse lines on the scapulas.

Fig. 7.—Marked involvement of the bones of the base of the skull as contrasted with those of the vault. The characteristic clubbing of the posterior clinoid process is seen.

Fig. 8.—The bones of the face are extremely heavy.

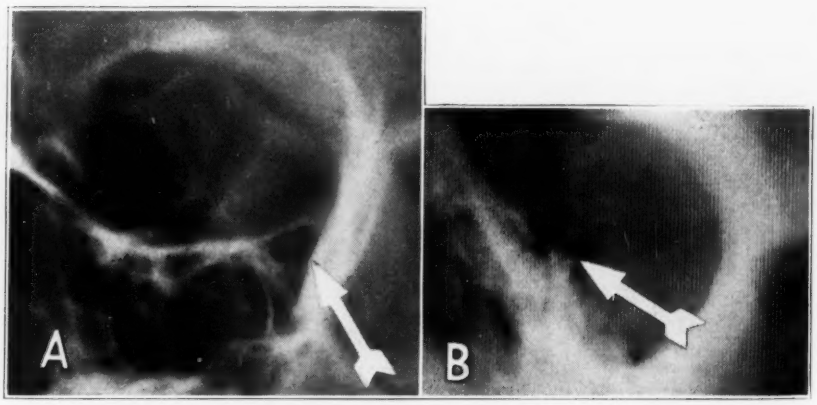

Fig. 9.—Normal optic foramen (*A*) contrasted with marked decrease in size of optic foramen of E. C. (*B*).

These specimens of bone were fixed in solution of formaldehyde, decalcified with a 5 per cent solution of nitric acid, embedded in pyroxylin and stained with hematoxylin and eosin.

In figures 12 and 13 are shown longitudinal sections from the right sixth rib. Figure 12 includes the costochondral junction and figure 13 shows a region farther costalward.

At the top of figure 12 are seen clusters of cartilage cells with stellate or oval nuclei and intervening hyaline matrix (*A*). The cartilage cells of the epiphysial

Fig. 10.—Roentgenogram of the chest taken on the tenth day of life, read as showing only an enlarged thymus. There is increased density of all the bones.

line are arranged in irregular columns; their nuclei are pyknotic, and the cytoplasm is vacuolated (*H*). The junction of cartilage columns with medullary tissue is irregular (*B*). Nowhere throughout the sections of rib shown here does one see a continuous marrow cavity; there are only irregular and isolated spaces or channels, which appear to parallel roughly the long axis of the bone. In the metaphysial region (*I*), as well as much farther from the epiphysis, are seen many acellular masses of homogeneous matrix (*C*); some of these masses contain

vacuolated cartilage cells (*D*). The borders of this matrix are scalloped and in some instances stain intensely (*E*). The marrow spaces thus enclosed are lined by endothelial or hemopoietic tissue (fig. 13, *F*). Cells isolated in the matrix are usually surrounded by an intensely stained zone (fig. 13, *G*). The amount of this deeply staining matrix increases as one looks costalward from the epiphysis (fig. 13). The marrow spaces are largely occupied by normal hemopoietic tissue or blood vessels.

There was a thin layer of subperiosteal bone that is not shown in either photomicrograph of rib. This layer was of irregular thickness and merged

Fig. 11.—The chest at the tenth week, after roentgen therapy for enlargement of the thymus. One sees the first line parallel to the epiphysis at the proximal end of the humerus. Density of bones is increased.

with the faintly stained matrix noted elsewhere in the costal sections. There were numerous lacunas in the bone, each occupied by a bone cell; there were no haversian systems, canaliculi or trabeculae, and the amorphous intercellular matrix resembled the more intensely stained areas shown in figure 12, *E*. No typical osteoblasts or osteoclasts can be seen in either of the sections shown here. The faintly stained ground substance (*C*) is the most plentiful constituent of both sections.

Figure 14 shows a cross section of tibia. This portion of bone was removed from the upper end of the tibia, making the defect shown in figure 3. At the

top of this photomicrograph one sees subperiosteal bone of the tibia (*A*). This bone is composed of a uniform basophilic matrix and numerous cell-containing lacunas. There are blood vessels (*B*), but no distinct haversian systems, canaliculi or laminations can be seen. Beneath the thin layer of cortical bone is a mass of tissue resembling the faintly stained ground substance found in the rib (*C*). This tissue, unlike the subperiosteal layer, contains isolated marrow spaces (*D*). There are numerous intensely stained zones, each surrounding a cell isolated in the matrix (*E*) or bordering on a marrow space (*F*); these intensely stained zones of matrix resemble the subperiosteal bony substance. The cellular elements occupying the marrow spaces are like those observed in the rib. No typical osteoblasts

Fig. 12.—Longitudinal section of the sixth rib on the right, including the costochondral junction (magnification, 130 diameters). *A*, clusters of cartilage cells and intervening hyaline matrix; *B*, irregular junction of cartilage columns with medullary tissue; *C*, acellular masses of homogeneous matrix; *D*, such masses contain vacuolated cartilage cells; *E*, borders of this matrix stain intensely; *H*, irregular columns of senescent cartilage cells.

or osteoclasts are seen in either the cortical or the spongy bone, nor is there any evidence of osteoblastic activity.

A chemical analysis of the cortical and of the spongy portion of bone showed that the latter had a somewhat higher ash content and that the specimens of ash from both portions of the bone were identical in composition. Estimation of the

phosphatase content of the two portions of bone showed that the spongy portion contained more phosphatase than the cortical portion and that both had little of this enzyme.

Type of Bone	Percentage Composition of Ash				Percentage of Ash in Fat-Free Bone	Phosphatase, Bodansky Units*
	Calcium	Phosphorus	Magnesium	Calcium-Phosphorus Ratio		
Cortical	40.2	17.7	0.31	2.26	65.0	1.00
Spongy	40.0	17.7	0.26	2.28	71.5	4.16
Rib	....	....	....	....	....	2.13

* Per gram of fresh bone.

TABLE 1.—*Study of the Calcium Balance of E. C. When He Was Receiving a Diet Low in Calcium*

Periods of 5 Days	Preparation Administered	Daily Dose	Total Calcium Intake, Mg.	Calcium Output, Mg.			Calcium Balance, Mg.+	Serum Calcium, Mg. per 100 Cc.	Serum Phosphorus, Mg. per 100 Cc.	Phosphatase, Units
				Urine	Feces	Total				
I	Control	.....	525.9	64.8	71.4	136.2	389.7	10.7	4.3	3
II	Control	.....	503.5	98.0	85.4	183.4	320.1			
III	Ammonium chloride	60 gr.	548.4	372.8	48.8	421.6	126.8			
IV	Ammonium chloride	120 gr.	531.3	212.8	109.1	321.9	209.4			
V	Thyroid	1 gr.	580.5	45.0	40.0	85.0	495.5			
VI	Thyroid	1 gr.	592.2	52.4	75.5	124.9	467.3	9.7		
VII	Thyroid	2 gr.	616.0	75.5	76.1	151.6	464.4	10.0	3.7	
VIII	Thyroid	3 gr.	576.9	81.6	101.8	183.4	393.5			
IX	Thyroid	6 gr.	621.0	105.0	81.7	186.7	434.3			
X	Thyroid	6 gr.	565.0	13.3	59.1	72.4	482.6	9.6	3.2	
XI	Thyrotropic substance	0.5 cc. every other day	523.3	14.9	53.1	68.0	455.3			
XII	Thyrotropic substance	5 cc. every other day	506.0	18.7	34.2	52.9	443.1			
XIII	Parathyroid extract	1 cc. or 100 (H) units	531.2	23.5	61.4	84.9	446.3	9.1	3.6	
XIV	Parathyroid extract	1 cc. or 100 (H) units	511.0	30.8	65.2	96.0	415.0			
XV	Parathyroid extract	1 cc. or 100 (H) units	556.5	75.5	67.5	143.0	413.5	9.6	3.5	

A study of the calcium balance was conducted to ascertain whether or not calcium could be withdrawn from the bones. The management and methods were carried out according to the technic of Bauer and Aub.[3] The low calcium diet offered 1,000 calories per day, or 66 calories per kilogram of body weight. By analysis this daily diet contained 0.1264 Gm. of calcium and 0.2999 Gm. of phosphorus. Each period of observation was five days.

In table 1 will be found the total calcium intake for each period and the calcium excretion in the urine and feces. The following facts will be noted:

3. Bauer, W., and Aub, J. C.: Studies of Inorganic Salt Metabolism: I. Ward Routine and Methods, J. Am. Dietet. A. **3**:106, 1927.

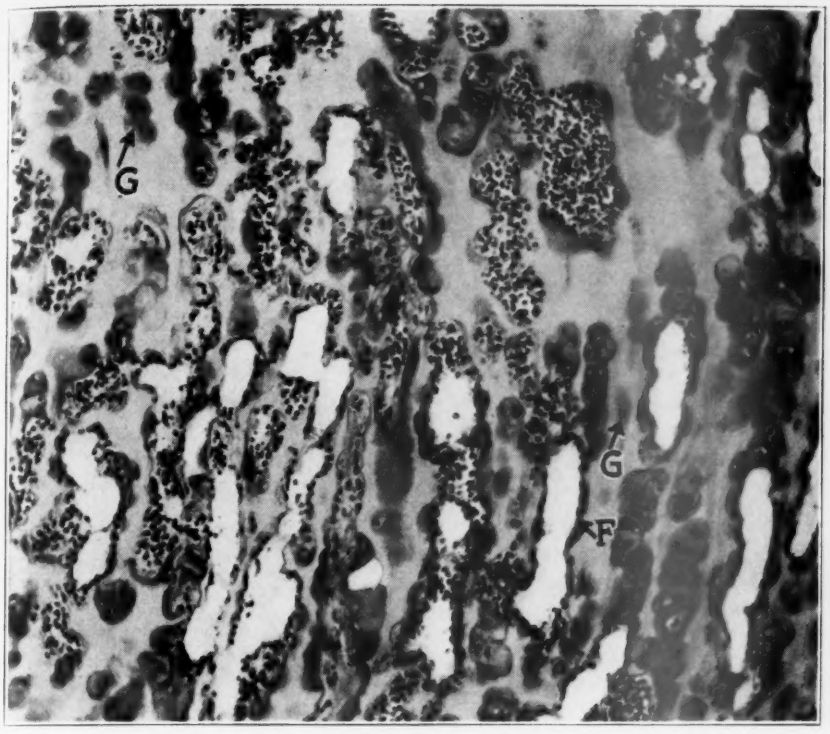

Fig. 13.—Longitudinal section of the sixth rib on the right, farther costalward than in figure 12 (magnification, 130 diameters). *F*, marrow space lined by endothelial tissue; *G*, cells isolated in the matrix surrounded by an intensely stained zone.

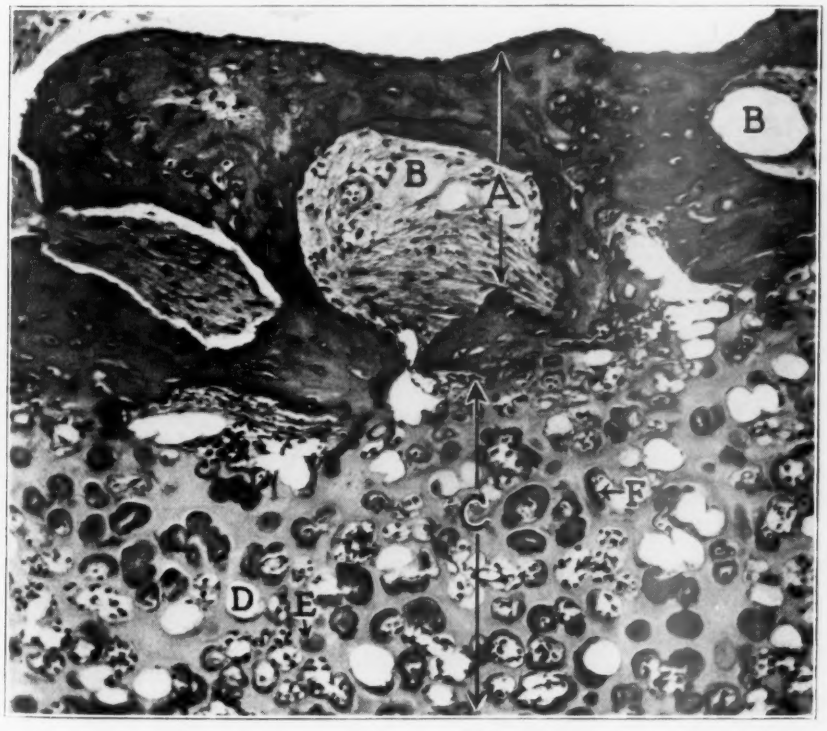

Fig. 14.—Cross section of the tibia (magnification, 130 diameters). *A*, subperiosteal bone (no distinct haversian systems, canaliculi or laminations seen); *B*, blood vessel; *C*, ground substance comparable to that in figure 12 *C*; *D*, isolated marrow space; *E*, intensely stained zones surrounding isolated cell in matrix or *F*, bordering on a marrow space.

1. The calcium balance was positive throughout the period of study. 2. Calcium retention was relatively high for a patient given a diet so low in calcium (above 50 per cent except on two occasions). 3. Urinary excretion of calcium was markedly greater than fecal excretion during the administration of ammonium chloride, but the difference was negligible or fecal excretion was greater during the remainder of the experiment. Thyroid in amounts up to 6 grains (0.39 Gm.) a day did not increase the loss of calcium. Parathyroid extract, 100 U. S. P. units per day, likewise did not produce the characteristic increase in urinary calcium. 4. The administration of large doses of ammonium chloride, thyroid, a pituitary extract containing the thyrotropic factor and parathyroid extract failed to influence the calcium and the phosphorus content of the serum.

COMMENT

The cause of osteopetrosis, or marble bones, is unknown. There is a decided familial tendency. McPeak [2i] has reported 8 cases occurring in three generations of one family, and Harnapp [2j] found diffuse osteosclerosis in a father and 5 of his 7 children. Parental [4] consanguinity has also been reported in several instances and is a factor to be considered with our patient. Generalized osteopetrosis is essentially a disease of childhood and is usually diagnosed during that period. The patient here reported on had roentgen evidence of marble bones on the tenth day of life; so one must conclude that the process began in utero. The transverse lines of greater and lesser density were present as early as the tenth week.

Almost all the features characteristic of marble bones were demonstrated in the case here reported; these include stocky build, square forehead, pigeon breast, bowed legs, atrophy of the optic nerves since early infancy, arrested dentition, constant purulent rhinitis with frequent infections of the respiratory tract and generalized increased density of the bones.

It was true here, as in the majority of cases of marble bones, that the diagnosis was made by roentgen study. The characteristic changes are as follows: The bones of the entire body show increased density with loss of normal structure. The shadow of the marrow cavity is reduced, sometimes even obliterated. The greatest density is seen in the vertebral

4. (*a*) McCune and Bradley.[2a] (*b*) Lorey and Reye: Ueber Marmorknochen (Albers-Schönbergsche Krankheit), Fortschr. a. d. Geb. d. Röntgenstrahlen **30**:35, 1923. (*c*) Alexander, W. G.: Report of a Case of So-Called "Marble-Bones" with a Review of the Literature and the Translation of an Article, Am. J. Roentgenol. **10**:280, 1923. (*d*) Kudrjawtzewa, N.: Ueber Marmorknochenkrankheit, Arch. f. klin. Chir. **159**:658, 1930. (*e*) Cohn, M., and Salinger, H.: Ueber ungewöhnliche Kalkanreicherung in den Gefässen und im Stützgewebe, Med. Klin. **23**:825, 1927. (*f*) Llado, C.: Contribution à l'étude de la maladie marmoréenne des os, Rev. d'orthop. **18**:740, 1931. (*g*) d'Istria, A.: Su di un caso di "Marmorknochen" malattia di Albers-Schönberg, Radiol. med. **15**:473, 1928. (*h*) Windholz, F.: Osteosclerosis fragilis generalisata (Marmorknochenkrankheit) mit periostaler Knochenneubildung, Ztschr. f. Kinderh. **51**:708, 1931.

bodies, in the central part of the pelvis, in the base of the skull and in the ends of the long bones.

In the present case there was broad and symmetric clubbing of the ends of the long bones. The proximal end of the humerus and the distal end of the femur (figs. 2 and 6) showed this particularly well. This clublike thickening invariably involves the posterior clinoid processes and causes a narrowing of the sella turcica (fig. 7). Some authors have insisted that this constitutes a pathognomonic sign of osteopetrosis. Narrowing of the optic foramina with consequent impingement on the optic nerves produces the atrophy of the nerves and the blindness. Similarly, there may be involvement of the auditory nerves or stenosis of the meatuses of the paranasal sinuses. The delay or arrest of dentition is probably due to sclerosis of the alveolar bone but may be due to some involvement of the tooth buds themselves.

The structure of the bones appears altered. There are alternating transverse bands of greater and lesser density parallel to the epiphysial lines of the long bones. These bands vary in width and number and sometimes, as in this instance, extend into the diaphysis. In the present case these were well demonstrated in the distal end of the femur (fig. 2), in the proximal end of the tibia and in the long bones of the hands and feet. These bands of varying density are arranged parallel to the epiphysial lines of the flat bones and give a fanlike appearance to the bones of the pelvis. Such changes usually occur very early in the tarsal bones.

In our patient there was such diffuse increased density that the sharply demarcated foci of compact bone sometimes referred to as occurring in the metacarpal and metatarsal bones were not seen.

The ossification centers appear at the normal time and, although involved in the sclerosing process, proceed to fusion with the shaft at the usual time. Longitudinal growth, however, is sometimes retarded, as illustrated here.

The bones are not only more dense than normal but also more brittle. This fragility leads to frequent and multiple fractures, which tend to be transverse and painless. However, when the periosteum is involved or when there is displacement of the fragments, pain and disability are present. Healing is usually accomplished in the normal length of time.

Metabolic studies have been made on 5 patients,[5] including the one here reported on. Our results paralleled those of the other observers

5. (*a*) McCune and Bradley,[2a] (*b*) Flood, R. G.: Calcium Metabolism in Marble Bone (Albers-Schönberg Disease), California & West. Med. **31**:203, 1929. (*c*) Laurell, H., and Wallgren, A.: Untersuchungen über einen Fall einer eigenartigen Skeletterkrankung (Osteosclerosis fragilis generalisata), Upsala läkaref. förh. **25**:309, 1920; abstracted, J. A. M. A. **76**:560 (Feb. 19) 1921. (*d*) Bernhardt, H.: Ein Beitrag zur Marmorknochenerkrankung (Albers-Schönberg'sche Krankheit), Klin. Wchnschr. **5**:415, 1926.

in that a positive calcium balance was maintained with diets high and low in calcium during the administration of ammonium chloride, thyroid and parathyroid extract. McCune and Bradley [2a] also reported a positive calcium balance with a diet containing vitamin D. There was likewise no change due to the administration of thyrotropic pituitary substance. Flood reported "a small negative balance" once during the administration of parathyroid extract. His patient had an elevation of the calcium content of the serum to 15 mg. per hundred cubic centimeters. The calcium and the phosphorus content of the serum were normal in other patients during the entire period of observation. The phosphatase content of the serum has been reported in 4 cases. In 3 [6] it was interpreted as slightly elevated and in the fourth [2b] as decidedly elevated. In the fourth case the patient also had osteogenic sarcoma, which is known to be associated with an increase in the phosphatase content of the serum. The opposite was true of our patient; determinations of the phosphatase content of serum and bone, both rib and tibia, were low.

The chemical composition of the bone ash in osteopetrosis as determined by our own observations and by those of others is within normal limits; however, we found the percentage of ash high for the more distinctly pathologic bone. Table 2 gives a comparison of the values according to those who have made analyses of bones of both normal children and children with osteopetrosis.

Variation in the peripheral blood picture has been found as well as extramedullary myelopoiesis or hemopoiesis. We have observed hypochromic anemia developing in our patient during the past year; this has not responded to iron therapy. As a general rule, however, the anemia does not parallel the progress of the sclerosis.

Changes are reflected in both the gross appearance and the physical properties of the bone. The bones have been found to be heavy, hard, thick and difficult to cut, with loss of elasticity. There is also a tendency for the bone to fracture rather than bend. Surfaces made by cutting the bones reveal a thickened substantia compacta and a substantia spongiosa of finely meshed trabecular structure, with little or no visible marrow cavity. The distinction between substantia spongiosa and substantia compacta is at times impossible to the naked eye. In Pirie's [7] case transverse lines resembling those caused by disturbance in growth were seen in the metaphyses of the bones about the knee joint.

Membrane bone, exemplified by the vault of the skull, has been described as made up of densely arranged trabeculae of spongy bone

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6. Ellis,[2b] Mayer, O. B., and Pitts, T. A.: Osteopetrosis: Report of a Case, J. A. M. A. **101**:22 (July 1) 1933.

7. Pirie, A. H.: The Development of Marble Bones, Am. J. Roentgenol. **24**:147, 1930; Marble Bones, ibid. **30**:618, 1933.

and has been found to be devoid of diploic structure.[8] Cortical bone[9] has been found to be thickened. Haversian systems, usually small, are distorted or show atypical branching of the haversian canals.

Apparently the hyaline matrix elaborated by the cartilage cells persists indefinitely, becomes highly calcified and is only partially replaced by marrow tissue or membranous bone. This results in unorganized amorphous bone without the normal amount of differentiation. The membranous bone formed is scanty, and its differentiation is imperfect; it is difficult to determine whether this is due to a persistence of calcified cartilage or to some defect in the formation of membranous bone. Perhaps an inability to form adult bone causes this much more primitive type to persist as a poor substitute. The difference in the intensity of staining in the proximity of cells isolated in the matrix suggests that some atypical osteoid tissue is being formed. Similar-appearing islands of

TABLE 2.—*Comparative Analysis of Bone Ash in Normal Children and in Children with Osteopetrosis*

Investigator	Subjects	Calcium, %	Phosphorus, %	Magnesium, %	Phosphatase, Bodansky Units
Schabad [2a]	Normal children	21.0-28.0	12.0-20.0	0.10	
Kapyloff [2a]	Girl with osteopetrosis, age 10 years	29.0	10.0	0.72	
Kudrjawtzewa [4d]	Girl with osteopetrosis, age 10 years	29.0	20.0		
Freeman	Boy, age 5 yr., our patient				
	Tibia, cortical portion	26.2	11.5	0.20	1.00
	Tibia, spongy portion	28.5	12.6	0.19	4.60
	Rib	....	....	....	2.13

cartilaginous matrix surrounded by osteoid tissue are frequently observed in the metaphysis during the healing of rickets. The persistence of hyaline matrix might be due to some abnormality either in the matrix itself or in the lytic mechanism. Whatever osteoid formation or lysis of matrix occurs does so in the absence of typical osteoblasts or osteoclasts. The last-mentioned deficiency is of particular interest in view of the failure of parathyroid extract to increase excretion of calcium. No doubt the marrow spaces are connected and form a circulatory system for the bone.

Dijkstra [8b] observed in studying a vertebra and rib of a 3 year old boy that from the resting cartilage up to the osteochondral junction the usual changes associated with the preparation of cartilage for ossification

8. (*a*) Madolny, G.: Diffuse Osteosklerose im Kindersalter, Jahrb. f. Kinderh. **105**:212, 1924. (*b*) Dijkstra, O. H.: L'ostéogénèse dans la maladie des os marmoréens, Ann. d'anat. path. **12**:131, 1935. (*c*) Laubman, W.: Ueber die Knochenstruktur bei Marmorknochenkrankheit, Virchows Arch. f. path. Anat. **262**: 23, 1935.

9. Dijkstra,[8b] Pirie,[7] Lauterberg, W.: Beitrag zur Kenntnis der Marmorknochenkrankheit, Schweiz. med. Wchnschr. **56**:441, 1926; Beitrag zur Kenntnis der Osteosclerosis fragilis generalisata, ibid. **58**:677, 1928.

occurred (fig. 12). Beyond this point incomplete resorption of the cartilaginous ground substance or primary osseous tissue took place (fig. 12). The osseous tissue progressively increased in amount and eventually predominated, although islands of cartilaginous material were present (fig. 13). Pirie [7] noted the same changes in the bones about the knee of a 14 year old girl. Laubman [8c] noted the same general plan of structure in the long bones, in the phalanges and in the bones he studied that were derived from cartilage. He and Pirie, moreover, described osteoblastic foci and all the stages of osteogenesis within the cartilaginous ground substance. In the diaphyses, not only were these changes present but there was metaplasia of fibrous marrow with formation of cartilage and bone.

The prognosis depends largely on the rapidity with which the sclerosis advances. In some cases in which the condition developed in utero there have been stillbirths. When osteopetrosis causes enough symptoms to be diagnosed during early infancy the expectancy of life is extremely short. Under the most favorable circumstances these patients are handicapped for adult life. The brittleness of the bones results in pathologic fractures, causing frequent periods of incapacity. Blindness or impaired vision, sometimes associated with subnormal mentality, increases the dependent status of the person with marble bones who does reach adult life. Apparently there are milder forms of the disease which are compatible with longevity and good health. Gortan [10] reported a case of osteopetrosis in a woman of 72 years. Death is usually due to intercurrent infection or to anemia.

As has been shown in the case here reported and in cases observed by others, there is no known specific treatment for osteopetrosis. Nothing has been found which will alter the condition in any way. Treatment therefore is directed toward relief of symptoms or care of the conditions secondary to osteopetrosis, most frequent of which are pathologic fractures.

SUMMARY

A case of osteopetrosis in a child of 5 years which began in utero is reported.

Roentgenologic, metabolic, chemical and histologic studies are reported. The results seem to support the prevailing opinion that osteopetrosis is a true developmental disease characterized by faulty differentiation of osseous and hematogenic tissue.

707 Fullerton Avenue.

10. Gortan, M.: Un caso di morbo di Albers-Schönberg, Boll. e mem. Soc. piemontese di chir. **2**:769, 1932.

MICROSEDIMENTATION OF THE ERYTHROCYTES IN INFANTS AND IN CHILDREN

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The sedimentation rate of the red blood cells is now universally considered a valuable guide for determining the presence of infection in the body. Many have found it a useful indicator of activity in cases of tuberculosis. Its value in cases of acute rheumatic fever has been repeatedly demonstrated [1] and it has become one of the physician's most reliable adjuncts in determining the probable cessation of activity and the duration of the period of rest for patients with this illness.

One of the disadvantages of this test, however, has been the need for withdrawing blood from the veins. The objections to this procedure are obvious in pediatric work. Children dread the pain. In obese patients and in infants it is often difficult to find a vein. Further, it is desirable to spare these vessels for more important therapeutic procedures. Since the value of the sedimentation test usually depends on repeating reading at frequent intervals, it has become desirable not only to simplify the technical steps involved in the actual test but to develop a method requiring minimal amounts of blood, which could be withdrawn from the tip of a finger as for the ordinary blood count. The further advantage of such a method would be to make the test available in routine office and home practice.

A number of instruments had already been devised when I began my search for a suitable micrometric apparatus; each type required some modifications of an existing macromethod, of which there were many. Landau [2] at first used capillary tubes with a bulb at one end, similar to the chamber in the blood cell pipets. He soon found that these tubes were unnecessarily long and that he could further simplify his method by reducing the length of his tubes to 12 cm. By the use of a special device he was able to draw a solution of citrate and blood directly into the capillary tube used for sedimentation. This would seem to be the ideal arrangement, but it required careful sealing of the

From the Abraham Jacobi Division for Children of the Lenox Hill Hospital, service of Dr. Jerome S. Leopold.

1. Clifton, W.: Erythrocytic Sedimentation in Rheumatic Infection, Am. J. Dis. Child. **52**:1093 (Nov.) 1936.

2. Landau, A.: Microsedimentation (Linzenmeier-Raunert Method), Am. J. Dis. Child. **45**:691 (April) 1933.

tip of the tube to prevent loss of the contained specimen in the vertical position.

Cutler [3] developed a micromethod which required 0.5 cc. of capillary blood, which was mixed in a small storage tube with 3 per cent sodium citrate and then drawn into the sedimentation pipet, the stem of which was 2.5 mm. in internal diameter and graduated in 50 mm. divisions, the capacity of the graduated portion being 0.3 cc. Considerable technical skill was required to apply a spring attachment to seal the bottom of the pipet so that the contained blood would not leak out. This would seem to be a real objection to the use of the apparatus.

Thus the main difficulty with these several procedures was that they were not, strictly speaking, micromethods, for they used tubes of unwieldy length and still withdrew blood from the veins, or they required some complicated little mechanism to retain the contained specimen during the sedimentation period.

To obviate these difficulties Smith [4] developed an apparatus [5] which utilized a tube similar to the Cutler tube but had several advantages: The equipment was compact, it required minimal samples of blood, obtainable by puncture of the finger as for the routine blood count, and it permitted the technic of its use to be easily acquired because of the simplicity of materials used and steps involved. Smith compared his micromethod for capillary blood with Cutler's macromethod for venous blood on an adequate number of cases. He obtained figures which compared satisfactorily for all practical purposes, the deviations being negligible; thus he assured himself of the reliability of his method.

In my previous work,[6] in which I used the Linzenmeier, Westergren and Cutler macrometric methods in parallel tests, I concluded that the Cutler tubes were the most practical and satisfactory for routine tests. In examining a micromethod with a view to replacing the macromethod in use, I therefore decided to use the Cutler method, with which I had become familiar, as a control. The Smith apparatus seemed to satisfy my requirements, and I planned to compare the method of using it with the Cutler macromethod. This, coincidentally, is precisely what Smith did.

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3. Cutler, J.: A Finger Puncture Method for the Blood Sedimentation Test, Am. J. M. Sc. **173**:687 (May) 1927.

4. Smith, C. H.: A Method for Determining the Sedimentation Rate and the Red Cell Volume in Infants and Children with the Use of Capillary Blood, Am. J. M. Sc. **192**:73 (July) 1936.

5. The Smith apparatus is obtainable from E. Machlett & Son, 220 East Twenty-Third Street, New York.

6. Rogatz, J. L.: The Comparative Value of the Schilling Differential Count and the Sedimentation of the Erythrocytes in Acute Rheumatic Fever in Childhood, J. Pediat. **8**:184 (Feb.) 1936.

Since the beginning of my work, a number of other micromethods have been reported; these, for one reason or another, do not appear quite as satisfactory as that involving the Smith apparatus. Frimberger [7] used pipets 100 mm. long. Though they required but 0.125 cc. of blood, they were comparatively complicated in structure, with a stopcock device to retain the blood in position. Steiger's apparatus [8] was too briefly described to permit of fair judgment; in any event, it is probably not available in this country. Brooks [9] described a pipet 100 mm. long, but also adapted for intravenous use, with a needle attached to one end and a stopcock at its base to permit blood to be drawn directly into the pipet in which the cells are allowed to sediment. Though this utilization of the tube into which blood is directly drawn seems at first a desirable simplification, it obviously requires venipuncture and is therefore not strictly a micrometric technic. Kanitz [10] used a tube 300 mm. in length to hold a column of blood 200 mm. long; this is similar to the Westergren macrometric tube, which is unwieldy because of its length.

APPARATUS AND TECHNIC

After examination of the available methods, it was decided to use the Smith apparatus in a series of cases to determine its practical accuracy for general use, with the hope of replacing the less satisfactory macrometric methods now in use.

The Cutler macrometric tube is 70 mm. long with an internal bore of 5 mm.; it is graduated from 0 to 40 mm. in single millimeter divisions. A 5 per cent solution of sodium citrate is placed in the tube up to a mark indicated at its base. Blood is then withdrawn from a vein with a syringe and added to the tube until the zero mark is reached. The blood and the citrate are well mixed, and the tube is allowed to stand. Readings are made at one-half hour and one hour intervals, the approximate normal figures being 5 mm. or less in one-half hour and 10 mm. or less in one hour.

The Smith micrometric apparatus consists (figure) of four parts. *A* is a pipet for drawing up capillary blood, similar to the Sahli pipet for determination of hemoglobin content. It has two graduations, one at 0.04 cc. and the other at 0.1 cc. The tube is long enough to permit capillarity within, thus retaining the blood after it has been drawn up. *B* is an ordinary small test tube for receiving the blood and mixing it with a solution of citrate. *C* is a long capillary pipet prepared from ordinary glass tubing, with an attached rubber bulb (similar to an elongated medicine dropper), the capillary portion being long enough to reach the bottom of the tube in which sedimentation takes place. *D* is a sedimentation

7. Frimberger, F.: Mikropipette zur Anstellung der Blutkörperchen-Sedimentierungs-Reaktion aus Fingerbeerenblut oder aus Venenblut, München. med. Wchnschr. **84**:25 (Jan. 1) 1937.

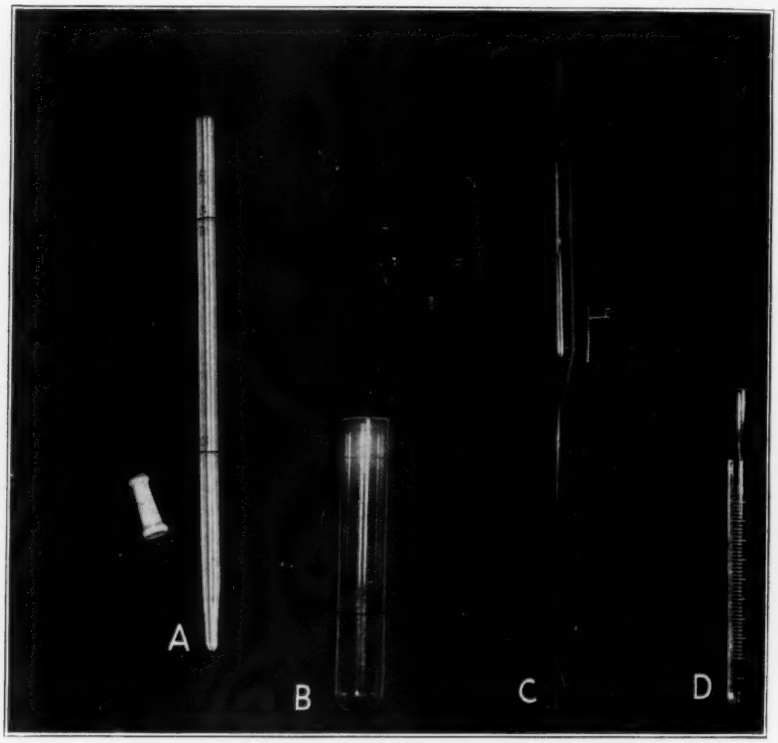
8. Steiger, V.: Ueber eine einfache Kleinausführung der Blutkörpersenkung, München. med. Wchnschr. **84**:939 (June 11) 1937.

9. Brooks, C.: A New Micropipet, Am. J. M. Technol. **3**:1 (Jan.) 1937.

10. Kanitz, H. A.: Ein neues Microsedimeter, Deutsche med. Wchnschr. **61**: 1929 (Nov. 29) 1935.

tube similar in length to the Cutler tube, having a diameter of 2.5 mm. and graduated in 50 mm. divisions, the capacity in the measured area being less than 0.25 cc.

The steps in the procedure are as follows: Pipet *A* is moistened within by drawing up a 5 per cent solution of sodium citrate several times and finally discarding all but 0.04 cc. This is expelled into test tube *B*; it is sufficient to prevent the clotting of 0.3 cc. of blood. The heel of an infant or the tip of a finger of an older child is punctured as for the usual blood count, and blood is taken up to the 0.1 cc. mark in pipet *A* and transferred to tube *B* three successive



The Smith microsedimentation apparatus, consisting of *A*, a pipet for drawing up capillary blood; *B*, an ordinary small test tube for receiving the blood mixing it with citrate solution; *C*, a capillary pipet for transferring the specimen to the sedimentation tube, *D*. Note that the capillary portion of the pipet, *C*, is sufficiently long to reach the bottom of the sedimentation tube, *D*.

times, care being taken to shake vigorously in order to secure thorough mixing of the blood and the citrate solution. The citrated blood is then carefully drawn up with pipet *C* and transferred to the sedimentation tube *D*. One can do this easily with little practice by inserting the capillary dropper to the bottom of the sedimentation tube and releasing the blood by gentle pressure on the bulb as the capillary portion is slowly withdrawn from the bottom of the tube until the uppermost zero mark is reached. At first it may seem difficult to avoid bubbles, but this problem in technic is solved after a few trials. The sedimentation tube

is then allowed to stand, and readings of the erythrocyte level are taken after one-half hour and one hour.

In the study reported here no attempts were made to read cell volume or to make other corrections, since the sole purpose was to determine the comparative readings of the respective methods under similar conditions. The error in each case would be the same and would not affect the comparative result.

TABLE 1.—*Normal Sedimentation Rates*

Case Number	Age, Years	Date	Diagnosis (Convalescent)	Cutler: Macromethod, Mm.		Smith: Micromethod, Mm.		Type of Blood
				½ Hr.	1 Hr.	½ Hr.	1 Hr.	
1	9	11/ 4/36	Cervical adenitis	4.0	8.0	2.0	6.0	Venous
3	6½	11/ 5/36	Catarrhal jaundice	2.5	8.0	1.5	5.0	Venous
7	10	11/11/36	Rheumatic endocarditis	3.0	9.0	1.0	5.0	Venous
8	10	11/14/36	Acute pharyngitis	3.0	10.0	3.0	7.0	Venous
10	10	11/19/36	Rheumatic endocarditis	4.0	8.0	3.5	7.0	Venous
11	12	11/20/36	Asthma	1.5	6.0	1.0	3.0	Venous
12	10	11/20/36	Chorea	1.0	2.5	1.0	2.0	Venous
13	7	11/21/36	Rheumatic endocarditis	2.0	6.0	1.0	4.0	Venous
18	5	12/ 1/36	Rheumatic fever	4.0	10.0	4.0	10.0	Venous
21	2	12/ 4/36	Nutritional anemia	1.0	7.0	1.0	4.0	Venous
22	10	12/ 7/36	Chorea	2.0	4.0	2.0	2.0	Venous
24	10	12/ 9/36	Rheumatic endocarditis	1.0	4.0	2.0	3.0	Venous
34	11	4/16/37	Pleural effusion	4.0	9.0	4.5	9.5	Venous
40	7	5/ 6/37	Rheumatic fever ?	2.0	6.0	2.0	5.0	Venous
41	13	5/ 8/37	Leukemia ?	1.0	3.0	1.0	2.0	Venous
42	7	5/11/37	Chorea	3.5	9.0	3.0	8.0	Venous
43	12	5/12/37	Rheumatic fever	2.0	7.0	2.0	6.0	Venous
44	10	5/18/37	Chorea	1.5	5.5	1.5	5.0	Venous
46	4	5/27/37	Tuberculous cervical adenitis	4.0	11.0	4.0	10.0	Venous
48	9	6/19/37	Chorea	4.0	11.0	2.5	3.0	Venous
58	5	10/11/37	Asthma	4.0	8.0	3.0	7.0	Capillary
59	6	10/11/37	Asthma	2.0	4.0	3.0	5.0	Capillary
60	5	10/12/37	Chorea	3.0	4.0	3.0	8.0	Capillary
61	11	10/22/37	Asthma	...	...	5.0	10.0	Capillary
				4.0	11.0	5.0	10.0	Venous
64	8	10/22/37	Asthma	...	...	4.0	7.0	Capillary
				3.0	3.0	6.0	14.0	Venous
66	4	10/28/37	No abnormality	1.0	2.0	2.0	3.0	Capillary
70	3	11/ 8/37	Asthma	6.0	11.0	5.0	10.0	Capillary
74	5	11/18/37	Asthma	3.0	7.0	3.0	7.0	Capillary
75	7½	12/ 7/37	Rheumatic endocarditis	3.0	8.0	2.0	7.0	Capillary
78	3	12/ 8/37	Possible tuberculosis	3.0	8.0	3.0	7.0	Capillary
79	1½	12/ 8/37	Possible tuberculosis	6.0	8.0	4.0	9.0	Capillary
80	10	12/11/37	Rheumatic fever ?	4.0	9.0	5.0	10.0	Capillary
83	9	12/29/37	Asthma	4.0	8.0	3.0	7.0	Capillary
88	9	1/ 7/38	Hyperpyrexia ?	1.0	5.0	1.0	5.0	Capillary
89	9	1/ 7/38	Hyperpyrexia ?	1.0	3.0	1.0	5.0	Capillary
95	10	1/18/38	Rheumatic endocarditis	2.0	10.0	3.0	8.0	Capillary

METHOD OF OBSERVATION

Suitable subjects were chosen at random from the patients admitted to the wards, whether acutely ill or apparently well. In the earlier tests (cases 1 to 57) venous blood was used for both the Culter macrometric and the Smith micrometric tubes. In several of the cases (61 to 64) figures obtained from venous blood used in the Cutler apparatus were compared with those obtained from venous blood and from capillary blood used in the Smith tubes, so that in these cases there were three sets of figures for comparison. In all the remaining cases values obtained from the use of venous blood in the Cutler tube were compared with values for capillary blood used in the Smith tube.

Seventy-five patients were examined; on these, 100 tests were done. Tests 49 to 52 inclusive, for example, were all done on 1 patient, an 8 year old girl with acute rheumatic fever. The successive tests done at frequent intervals showed both the gradual reduction of the rapid rate to an almost normal level during a two month period of convalescence and the close correspondence of results with both methods. Among the 75 patients studied there were 36 with normal rates (tables 2 and 3). The patients were evenly divided according to sex. The ages ranged between 18 months and 13 years. The pathologic states examined were, as indicated in the accompanying tables, those likely to appear in the general pediatric service of a large hospital. The tests were performed by various members of the intern staff, who were assigned to laboratory procedures from time to time, the work being taken over by a new member every third month. In each case the first results were discarded until proficiency and reliability had been acquired in the newer technic.

RESULTS

A comparison of normal values is shown in table 2. Comparing his results obtained in his own tubes with those he obtained in Cutler's

TABLE 2.—*Comparison of Normal Sedimentation Values Obtained by Different Methods*

Method	Average Sedimentation Rate at ½ Hour (Smith) Mm.	Average Sedimentation Rate at ½ Hour (Rogatz) Mm.
Macromethod (Cutler)	3.9	2.8
Micromethod (Smith)	4.3	2.7
	Average Sedimentation Rate at 1 Hour (Smith)	**Average Sedimentation Rate at 1 Hour (Rogatz)**
Macromethod (Cutler)	8.6	7.0
Micromethod (Smith)	9.1	6.3

macrometric tubes, Smith found the average sedimentation at the end of one-half hour to be 4.3 mm. in his own tubes and 3.9 mm. in Cutler's tubes; at the end of one hour Smith's tubes showed 9.1 mm. and Cutler's 8.6 mm. Thus the figures obtained from the Smith tubes were in each case slightly higher than those obtained from the Cutler tubes.

The results of observations made by my associates and me were reversed in that our normal values for both sets of tubes were slightly lower than Smith's. Thus our average normal value at the end of one-half hour with the Cutler tubes was 2.8 mm., whereas Smith obtained 3.9 mm.; with the Smith tubes, 2.7 mm., whereas Smith obtained 4.3 mm.; at the end of one hour, with the Cutler tubes, 7.0 mm., whereas Smith obtained 8.6 mm., and with the Smith tubes, 6.3 mm., whereas Smith obtained 9.1 mm. These variations were not sufficiently great to influence the practical accuracy of the results obtained. All observers have found that a normal sedimentation value lies within 5 mm. at the end of one-half hour and within 10 mm. at the end of one hour.

TABLE 3.—*Rapid Sedimentation Rates*

Case Number	Age, Years	Date	Diagnosis	Cutler: Macromethod, Mm.		Smith: Micromethod, Mm.		Type of Blood
				½ Hr.	1 Hr.	½ Hh.	1 Hr.	
2	11	11/ 4/36	Acute rheumatic fever	7.0	17.0	7.0	13.5	Venous
4	11	11/11/36	Rheumatic endocarditis	5.0	11.0	4.5	11.0	Venous
5	11	11/11/36	Bronchitis	20.0	25.0	18.0	25.0	Venous
6	11	11/11/36	Acute rheumatic fever	8.5	14.0	7.0	14.0	Venous
9	11	11/19/36	Acute rheumatic fever	9.0	17.0	8.0	14.0	Venous
14	5	11/21/36	Acute rheumatic fever	15.0	22.0	12.0	18.0	Venous
15	12	11/28/36	Acute rheumatic fever	29.0	30.0	34.0	35.0	Venous
16	10	11/30/36	Rheumatic endocarditis	5.0	13.0	4.0	11.0	Venous
17	11	11/30/36	Rheumatic endocarditis	7.0	13.0	5.0	12.0	Venous
19	11	12/ 2/36	Chronic tonsillitis	8.0	18.0	7.0	14.0	Venous
20	9	12/ 4/36	Typhoid fever	5.0	10.0	4.0	13.0	Venous
23	2	12/ 8/36	Acute tonsillitis	19.0	25.0	19.0	24.0	Venous
25	10	12/12/36	Acute rheumatic fever	16.0	25.0	9.0	17.0	Venous
26	11	12/12/36	Acute rheumatic fever	8.0	17.0	6.0	14.0	Venous
27	9	12/14/36	Rheumatic pericarditis	28.0	34.0	31.0	31.0	Venous
28	3	3/ 3/37	Tuberculosis	10.0	16.0	9.0	16.0	Venous
29	13	3/ 3/37	Rheumatic endocarditis	9.0	15.0	6.0	12.0	Venous
30	10	3/15/37	Rheumatic endocarditis	12.0	21.0	8.0	15.0	Venous
31	10	3/23/37	Rheumatic endocarditis	29.0	31.0	27.0	32.0	Venous
32	10	3/30/37	Rheumatic endocarditis	27.0	28.0	30.0	31.0	Venous
33	10	3/30/37	Rheumatic endocarditis	28.0	31.0	28.0	32.0	Venous
35	6	4/19/37	Acute appendicitis ?	12.0	18.0	11.0	16.0	Venous
36	6	4/23/37	Cervical adenitis	29.0	32.0	30.0	33.0	Venous
37	7	4/21/37	Rheumatic endocarditis	6.0	12.0	6.0	12.0	Venous
38	12	4/28/37	Acute appendicitis ?	3.0	13.0	4.0	15.0	Venous
39	7	5/ 6/37	Pleural effusion	23.0	27.0	20.5	27.0	Venous
45	7	5/27/37	Rheumatic endocarditis	29.0	31.0	30.0	32.0	Venous
47	10	6/ 1/37	Rheumatic endocarditis	28.0	30.0	28.0	30.0	Venous
49	8	6/22/37	Acute rheumatic fever	23.0	26.0	23.0	27.0	Venous
50	8	6/27/37	Acute rheumatic fever	19.0	25.0	15.0	23.0	Venous
51	8	7/ 6/37	Acute rheumatic fever	14.0	19.0	14.0	24.0	Venous
52	8	8/ 2/37	Acute rheumatic fever	6.0	20.0	6.0	18.0	Venous
53	10	8/ 2/37	Acute rheumatic fever	6.0	18.0	6.0	18.0	Venous
54	9	8/ 9/37	Acute rheumatic fever	5.0	13.0	4.0	15.0	Venous
55	10	8/23/37	Acute pharyngitis	18.0	21.0	20.0	26.0	Venous
56	10	8/31/37	Acute pharyngitis	13.0	18.0	11.0	15.0	Venous
57	5	9/23/37	Acute tonsillitis	14.0	20.0	8.0	15.0	Venous
62	12	10/23/37	Acute rheumatic fever ?	12.0	21.0	10.0	17.0	Venous
						9.0	16.0	Capillary
63	12	10/25/37	Pulmonary tuberculosis	18.0	20.0	12.0	18.0	Venous
						13.0	19.0	Capillary
65	10	10/27/37	Smallpox vaccination	10.5	20.0	11.0	18.0	Capillary
67	10	11/ 1/37	Smallpox vaccination	6.0	13.0	3.0	11.0	Capillary
68	12	11/ 4/37	Acute rheumatic fever	10.0	19.0	9.0	16.0	Capillary
69	10	11/ 5/37	Acute rheumatic fever	12.0	24.0	16.0	25.0	Capillary
71	7	11/ 9/37	Pleurisy	7.0	13.0	7.0	12.0	Capillary
72	3	11/12/37	Pulmonary tuberculosis	7.0	17.0	0.0	0.0	Capillary
73	7½	11/17/37	Bronchopneumonia	11.0	20.0	8.0	15.0	Capillary
76	2½	12/ 7/37	Acute bronchitis	23.0	28.0	26.0	31.0	Capillary
77	10	12/ 7/37	Bronchopneumonia	13.0	16.0	12.0	15.0	Capillary
81	11	12/16/37	Appendicitis ?	5.0	9.0	6.0	13.0	Capillary
82	10	12/17/37	Acute rheumatic fever	26.0	29.0	18.0	29.0	Capillary
84	8	12/29/37	Acute rheumatic fever	14.0	22.0	9.0	14.0	Capillary
85	8	1/ 1/38	Bronchopneumonia	6.0	10.0	7.0	12.0	Capillary
86	10	1/ 6/38	Acute rheumatic fever	25.0	29.0	24.0	30.0	Capillary
87	10	1/ 6/38	Bronchopneumonia	13.0	23.0	10.0	17.0	Capillary
90	8	1/12/38	Acute nephritis	22.0	26.0	19.0	25.0	Capillary
91	10	1/14/38	Bronchopneumonia	15.0	24.0	11.0	21.0	Capillary
92	2½	1/17/38	Acute tonsillitis	21.0	24.0	14.0	17.0	Capillary
93	10	1/18/38	Acute rheumatic fever ?	7.0	15.0	6.0	13.0	Capillary
94	10	1/18/38	Rheumatic endocarditis	10.0	17.0	9.0	15.0	Capillary
96	9	1/24/38	Tuberculosis ?	3.0	11.0	3.0	11.0	Capillary
97	6	1/25/38	Bronchopneumonia	19.0	28.0	20.0	23.0	Capillary
98	6	1/26/38	Acute bronchitis	14.0	17.0	8.0	14.0	Capillary
99	10	1/26/38	Acute rheumatic fever	7.0	12.0	6.0	12.0	Capillary
100	5½	1/28/38	Bronchopneumonia	31.0	31.0	28.0	31.0	Capillary

In many of the cases the results were almost identical (cases 3, 4, 12, 18, 28, 34, 37, 40, 42, 44, 46, 71, 74, 78, 88, 96 and 99). Discrepancies increase naturally among the higher figures, which indicate more rapid rates, as, for example, in case 15. But here a variation of 5 mm. is not so significant as it would be in the case of a normal subject. The occasional complete failure of a test to give results is difficult to explain, as in case 72. The subject was under observation for pulmonary tuberculosis; no sedimentation was visible in the Smith tube, while a rapid rate was noted simultaneously in the Cutler tube. Cases 88 and 89 represent morning and evening tests made on the same patient, who had unexplained hyperpyrexia with a temperature of 106 F. During this state the sedimentation rates with both methods proved to be normal. To be sure there was no error in technic to account for this bizarre result, I personally repeated the evening tests, obtaining almost exactly the same normal values. The occasional failure of the sedimentation test to indicate a febrile state is not understood and is not in point in this discussion. The significant fact is that both micrometric and macrometric tests were reliable in that they gave similar readings. As can be seen from the tables, comparative figures for all tests by both methods, regardless of the kind of blood used, were identical in many cases and were sufficiently alike in most other cases to justify the use of the micrometric method as accurate and reliable.

SUMMARY

With the desire to replace the less advantageous macrometric tests for sedimentation rate by an equally accurate micrometric method requiring capillary blood, a series of comparative studies was made on 75 infants and older children between the ages of 18 months and 13 years. Thirty-six of the subjects were apparently well, the remainder being ill with various acute or chronic infections. The tests used for comparison were the Cutler macrometric method, which requires the use of venous blood, and the Smith micrometric method, with which capillary blood is utilized. Many of the experiments were done on the same specimen of venous blood with both tubes. In others venous blood was used for the Cutler tubes and venous and capillary blood, taken at the same time, were used for the Smith tubes.

One hundred readings involving two or more sets of tubes were done. The Smith apparatus was found to be 95 per cent accurate with the already proved Cutler macrometric method as a basis for comparison. In one of the 5 cases in which an appreciable discrepancy occurred there was a complete failure of the red cells to sediment at all in the Smith tube, a freakish accident not easily explained. In the other 4 cases rapid sedimentation was indicated despite the disparity

of the figures, so that the failure was one of degree rather than of fact. Even in these cases active infection was indicated; thus, since the test's main value is qualitative rather than quantitative, the Smith tubes were practically 99 per cent accurate. My associates and I therefore feel justified in substituting the simpler and more advantageous Smith micrometric test for the more difficult macrometric methods still in use.

SUMMARY AND CONCLUSIONS

The Smith micrometric method was compared with the accepted Cutler macrometric method in 100 tests, performed during a period of fourteen months by different workers on 75 infants and older children of varying ages and with different illnesses. On the basis of the results, it is concluded that the micrometric method, which requires minimal amounts of capillary blood, obtainable by pricking the finger, is a satisfactory test, is easy to use and is completely reliable in its accuracy. One need not hesitate to replace existing macrometric methods with this test.

TETANY SYNDROME IN NEWBORN INFANTS

REMOTE DEPOSIT OF CALCIUM SALTS FOLLOWING INJECTION OF CALCIUM GLUCONATE

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The local precipitation of calcium salts following intramuscular injection of calcium gluconate during treatment of tetany in newborn infants has been reported several times. So far I have seen no paper which mentions the occurrence of abnormal deposits within the body at a place remote from the original site of injection. Because of the rather frightening possibilities that such an eventuality affords, it is my purpose here to report 2 cases in which this phenomenon was observed.

The 2 papers that have come to my attention to date which record in detail the local deposit of calcium salts after injection of calcium gluconate are those of von Hofe and Jennings [1] and Tumpeer and Denenholz.[2] The former authors reported that calcium gluconate was introduced into both thighs and into the left infrascapular region. Calcium precipitation occurred in all three areas, and in the thighs sloughs developed, from which a green streptococcus was recovered. Gradual resorption was complete by the age of 2 months and 3 weeks. The latter authors also reported that sloughs developed, from which a chalky mineral substance was extruded. This was identified as calcium phosphate. Both calcium gluconate and calcium levulinate had been administered. Recently Bakwin [3] mentioned having seen this phenomenon occur, and I have observed it at least a half-dozen times. The occurrence is therefore probably far from rare.

REPORT OF CASES

CASE 1.—The patient, a boy, was born by low forceps delivery after difficult labor. During the course of treatment of severe tetany with associated general and cerebral edema, 10 cc. of a 10 per cent solution of calcium gluconate was injected into the muscles of the right thigh. The early soft swelling that this induced

1. von Hofe, F. H., and Jennings, R. E.: Calcium Deposition Following the Intramuscular Administration of Calcium Gluconate, J. Pediat. **8**:348 (March) 1936.

2. Tumpeer, I. H., and Denenholz, E. J.: Calcium Deposit Following Therapeutic Injections in Tetany of the New Born, Arch. Pediat. **53**:215 (April) 1936.

3. Bakwin, H.: Pathogenesis of Tetany of the New Born, Am. J. Dis. Child. **54**:1211 (Dec.) 1937.

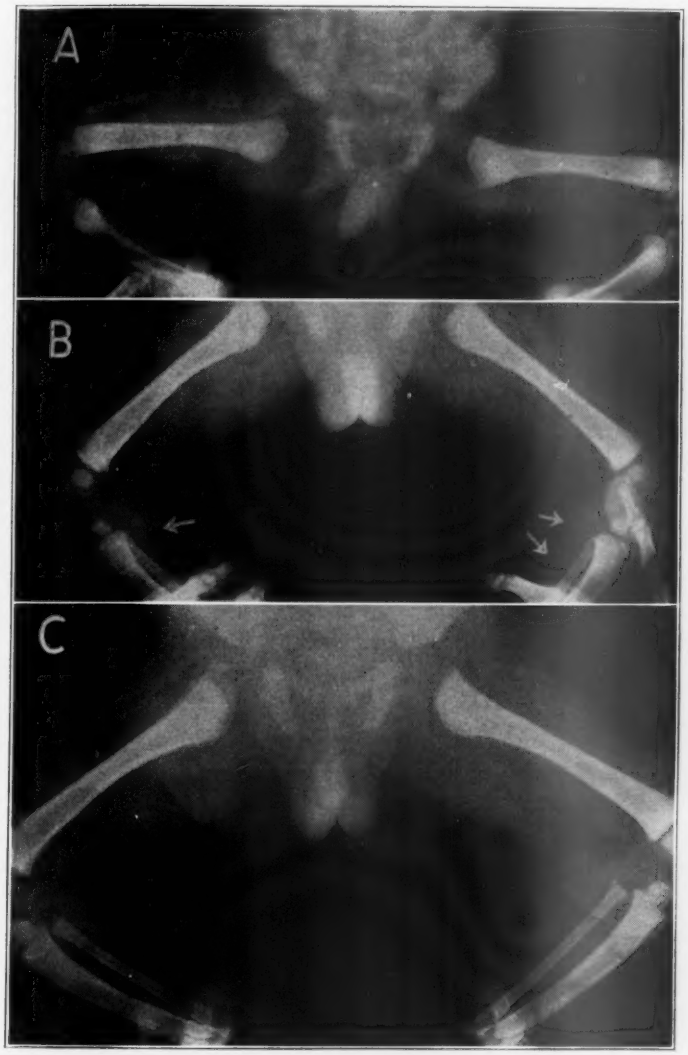

Fig. 1 (case 1).—*A*, roentgenogram showing the deposits of calcium throughout the muscles of the right thigh on the twenty-seventh day of life, nineteen days after the intramuscular injection of 10 cc. of a 10 per cent solution of calcium gluconate. *B*, roentgenogram taken thirty-five days after *A*, showing almost complete absorption of the calcium from the right thigh. The arrows point to blood vessels about both knee joints, visible presumably because of the deposits of calcium salts within their coats. Scattered deposits of calcium along the shaft of the left femur may or may not be within the blood vessels of this region. *C*, roentgenogram taken two months and five days after *B*. Precipitated calcium is no longer demonstrable.

was gradually replaced by an almost stony hardness, which persisted long after the tetany syndrome was under control. A total of 5.25 cc. of parathyroid extract had been injected over the period between the fourth and the fifteenth day. This had been reenforced by the oral administration of dicalcium phosphate ($CaHPO_4$) from the fourth day on. Administration of halibut liver oil with viosterol was started on the fourteenth day.

When the infant was 26 days old, nineteen days after the calcium gluconate was administered, roentgen study showed that this hard mass contained calcium salts, which were spread throughout the muscles of the right thigh. About one month later the tissues had returned to normal from a clinical standpoint, but roentgen examination showed the persistence of a small amount of precipitate near the hip joint.

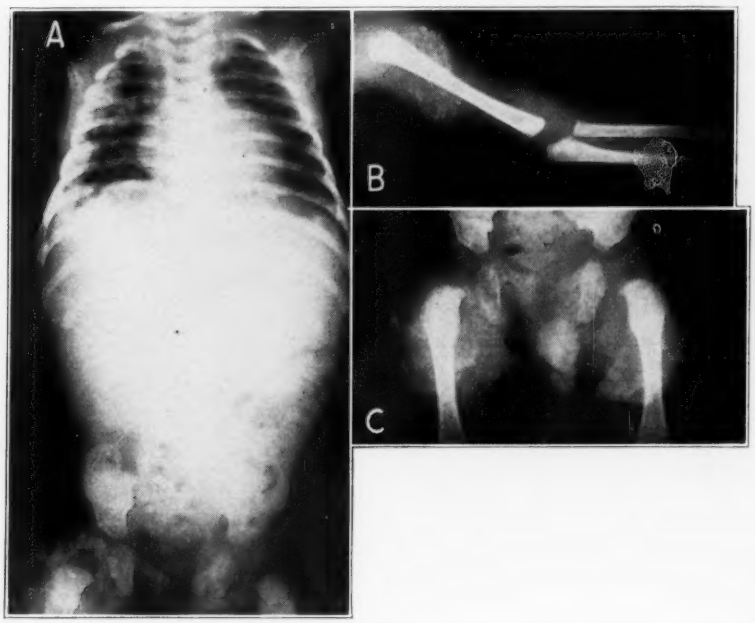

Fig. 2 (case 2).—*A* shows the massive deposits of calcium salts beneath the pleura and within the substance of the right lung and possibly at the base of the left lung. The roentgenogram was taken on the thirty-fifth day of life, thirty days after the last injection of calcium gluconate. *B*, local precipitation of calcium in the left deltoid region. *C*, precipitation of calcium in both gluteal regions. Roentgenograms *B* and *C* were taken forty days after the last injection of calcium gluconate.

At this time it was noticed that the arteries above and below both knee joints could be visualized, and the only possible explanation seemed to be that precipitation of calcium salts had occurred within the arterial coats. Other regions of the body were normal. Two months and one week later this deposit had apparently disappeared, since it could no longer be shown by roentgen study, and at the time of writing the patient, at the age of 4½ years, is an apparently normal boy. Blood calcium values were 6, 8, 13 and 10 mg. per hundred cubic centimeters on the ninth, tenth, eleventh and fourteenth day, respectively.

CASE 2.—The patient, a boy, was born by difficult forceps delivery. A tetany syndrome of extreme degree developed on the second day. As the disease was obstinate, a total of 35 cc. of calcium gluconate was injected intramuscularly over a period of four days and a total of 10 cc. of parathyroid extract (Lilly) within twelve days. One drop of purified vitamin D in propylene glycol (Drisdol) was given in the feeding every three hours from the sixth day on. Oral administration of 10 grains (0.65 Gm.) of calcium lactate every three hours was started on the tenth day. The spinal fluid at the beginning of the fourth day was clear and contained no cellular elements or excess of globulin. The calcium content was 2.2 mg. per hundred cubic centimeters, in spite of the fact that 20 cc. of calcium gluconate and 4 cc. of parathyroid extract had been given within the previous forty-eight hours.

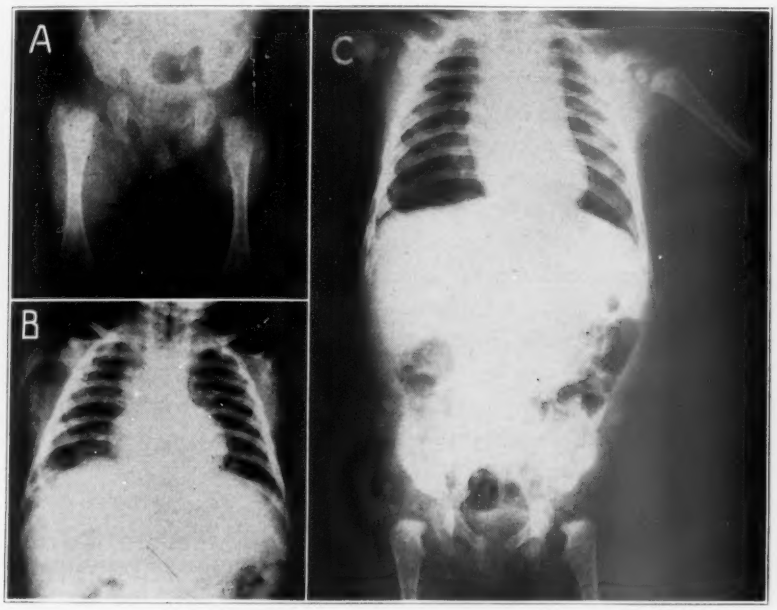

Fig. 3 (case 2).—*A*, partial absorption in the gluteal regions, and *B*, partial absorption in the lungs fifty-eight days after the last injection of calcium gluconate. *C*, complete absorption in all areas at the age of 5½ months. The thymus is markedly enlarged.

As in case 1, at all the sites of injection of calcium the early soft swelling gradually changed to a stony hardness with eventual sloughing. All four extremities were involved, and when the patient was 1 month old roentgen examination demonstrated calcium precipitation in each area.

At the same time the startling observation was made that a rather massive deposit of calcium was present in the substance of the right lung. There were no clinical signs by which its presence could have been recognized. Ten days later this precipitate was essentially unchanged. The blood calcium value was 12.2 mg. The sloughs in the extremities gradually healed, some with the extrusion of a chalky mineral substance. This was identified as calcium phosphate. The calcium deposits, both local and remote, were slowly absorbed, and by the time

the child was 5 months of age they had entirely disappeared. There was never any roentgen evidence of arterial involvement in this case.

COMMENT

The possibility that remote precipitation of calcium will follow the local injection of soluble calcium salts lends an aspect to the problem of treatment which would not be present were the only consideration that of a purely local lesion at the introductory site. While the dangers of local scarring, of sepsis and of other complications merit serious thought, they do not compare in significance with the dangers that might result from the deposition of calcium in arteries, lungs, kidneys or other organs vital to continued existence and development. Fortunately, the process of precipitation is apparently reversible in its action, since in both of these cases absorption ultimately took place.

Tumpeer and Denenholz [2] speculated at some length on the mechanism by which calcium that was injected in the form of the gluconate and the levulinate was precipitated as the phosphate. They felt it to be "possible that this precipitation process reflects the calcium derangement in tetany" and that "whatever the mechanism may be for the production of tetany . . . there is a failure of absorption and ionization from natural or artificial deposits." Their opinion derives added impetus from the recent report of Bakwin,[3] in all of whose cases there was a markedly increased phosphorus content of the blood serum. While it is not my opinion that all newborn infants with tetany must have a low value for blood calcium combined with a high value for phosphorus, Bakwin's work as well as a case reported by Farr [4] showed at least that this is not uncommon. In such instances, perhaps the local deposit of calcium phosphate should not be surprising. The explanation as to why some newborn infants with tetany do and others do not show the local precipitation of calcium salts after the intramuscular injection of calcium gluconate may well center around this very point. A greater theoretic significance, however, is to be found in the application of Bakwin's findings to the remote deposition of calcium salts. If it is this tendency to accumulation of phosphorus in the newborn period that is responsible for the local precipitation of calcium phosphate after the intramuscular injection of the gluconate or the levulinate, then it may well underlie a similar phenomenon at remote portions of the body.

Regardless of whether or not this is the underlying chemical mechanism, it is an undubitable fact that the possibility of a remote deposition of calcium salts greatly complicates the entire subject of the tetany

4. Farr, L. E.: Tetany of the New Born, Yale J. Biol. & Med. **9**:333 (March) 1937.

syndrome in the newborn. The manner of its occurrence is purely speculative. The rather massive accumulations that were present in the lung in case 2 were remarkably reminiscent of the localized deposits seen in xanthomatosis. The latter apparently are a result of an active process on the part of the cells of the reticuloendothelial system, by which they retrieve an excess of the lipoid substances present in the circulating fluids of the body. Such a conception is probably rather fantastic in this instance, however, since none of the many aberrant calcifications in the body is known to be a result of cellular activity. A more logical explanation, following the theories of Albright and his associates,[5] assumes that supersaturation of the body fluids with calcium phosphate has occurred. The factor which determines the locality in which such a deposit shall take place may well be some form of cellular injury, as has been suggested by Steck and others[6] in regard to extraosseous calcification that may occur as a result of hypervitaminosis D.

In any event, the possible by-effects are too varied to mention. They would depend on many factors: whether the precipitate was permanent or transient; whether or not the tissues involved were damaged thereby, and finally whether or not such damage, if it occurred, was reparable. So far as my associates and I were able to see in the 2 cases reported here, the calcium salt was eventually reabsorbed. This implies at least that the injury was relatively temporary. It indicates that the blood vessels resumed their original elasticity (if indeed they ever lost it) and that the parenchymatous cells of the liver, pancreas, kidneys and other organs, if they were injured, eventually assumed their normal function. However, according to what is now considered to be fact, such resumption would probably be impossible if the injured cells happened to be those of the central nervous system. Thus permanent damage might have occurred to the brain and /or the spinal cord had calcium been deposited there, even though eventual absorption became complete.

The remote precipitation of calcium salts after treatment of tetany of the newborn brings a new and acute problem into the limelight, namely, what shall be considered as the safe procedure in active treatment. Heretofore it has seemed primarily advisable to raise the level of the blood calcium in the most rapid way. The methods employed have included the injection of such salts as calcium gluconate and calcium levulinate either intramuscularly or intravenously, the feeding of

5. Albright, F.; Bauer, W.; Claflin, D., and Cockrill, J. R.: Studies in Parathyroid Physiology: The Effect of Phosphate Ingestion in Clinical Hyperparathyroidism, J. Clin. Investigation **11**:411 (March) 1932.

6. Steck, I. E.; Deutsch, H.; Reed, C. I., and Struck, H. C.: Further Studies on Intoxication with Vitamin D, Ann. Int. Med. **10**:951 (Jan.) 1937.

any of the usual calcium salts, the oral administration of vitamin D (or its essential equivalent, ultraviolet radiation) and the injection of parathyroid extract. The constant administration of carbon dioxide has seemed important to me, though it seems to have attracted little attention from other writers. Intramuscular injection of calcium gluconate has been shown frequently to result in the local deposit of calcium, often with sloughing of the tissues. This is an undesirable effect which in the cases that have so far come to my attention was not as serious as the condition that was being treated and seemed therefore to be condoned. To overcome this objectionable result, Bakwin advised that this salt be administered only by the intravenous route. Such a procedure has seemed to be an adequate protection against the local lesions that intramuscular injections might initiate, but one wonders whether or not it would be effective in avoiding a remote deposit. Precisely the same question is involved in the oral administration of calcium. Thus the safety of administering calcium in any form becomes a question of paramount importance.

Bakwin treated 2 of his patients with viosterol alone. A third was not treated at all, but that patient showed no active evidence of tetany. In all 4 recovery was prompt, much more so than I can believe would have been the case in any of my series in which the diagnosis was tetany of the newborn. I have seen many newborn infants who had symptoms suggesting this condition get well without treatment of any kind. But in such instances tetany has been considered only as suggested, and the cases add perhaps to my conviction that the condition is of frequent occurrence in newborn though often evanescent. Yet it has been my indisputable experience that usually when administration of viosterol is started there is a temporary increase in the manifestations of tetany in the infant. For this reason it has become my practice to omit the addition of vitamin D until the tetany is largely under control. It therefore becomes highly questionable whether the administration of vitamin D alone can generally be considered as reliably adequate treatment in these cases.

There remains for discussion the use of parathyroid extract. I have felt that this is the most dependable of all the factors important in the treatment of the tetany syndrome in the newborn and have employed it extensively. I cannot agree with many of the more recent writers who have stated that they would restrict the diagnosis of tetany in the newborn to infants with a low level of blood calcium,[7] but from the beginning I have recognized that parathyroid deficiency is probably

7. Bakwin.[3] Farr.[4] Guild, H. G.: Tetany of the New Born, Internat. Clin. **3**:46 (Sept.) 1933. Greenwald, H. M., and Palinsky, M.: Tetany of the New Born, Acta pædiat. **17**:386, 1935.

the principal cause in one class of cases.[8] For this group at least administration of parathyroid extract should be the treatment of choice. That it is extremely effective even in cases in which blood calcium values are normal or but slightly lowered I have had abundant opportunity to observe. Furthermore, in the large number of cases in which no chemical examination has been made, the precise cause of the condition therefore being left in doubt, I have rarely seen it fail to effect a definite, if sometimes transient, improvement.

It is for the very type of patient to whom Bakwin and others would restrict the diagnosis of tetany of the newborn, namely, those in whom there is an obvious parathyroid deficiency, that parathyroid extract should be most effective. Bakwin noted a low value for calcium combined with a high value for phosphorus in the blood of his patients. What could be more effective as a therapeutic agent than a substance the physiologic effect of which is precisely to cause rapid urinary elimination, with lowering of the blood phosphorus level, while at the same time it increases the calcium content in the blood? Since precisely this effect is produced by parathyroid extract,[9] it would seem evident that this substance should be the agent of choice, especially in cases of tetany due to parathyroid deficiency. The necessity of recognizing this fact would seem to be more urgent now that the possible precipitation of calcium salts out of the blood into various tissues of the body has become a reality. In fact, it becomes theoretically questionable whether any other means for raising the calcium level in the blood should be employed until parathyroid extract has been given in doses sufficient to gain active, even if temporary, control of the disease. Such speculation becomes mere guess work, of course, until a much wider experience has been gained with this complication under circumstances which permit accurate and detailed chemical studies.

SUMMARY AND CONCLUSIONS

Two cases are presented in which, complicating the treatment for severe tetany of the newborn, calcium salts were precipitated not only at the site of local injection of calcium gluconate but at remote points in the body.

Reabsorption eventually occurred without known permanent damage.

If this can occur after the local injection of calcium salts, there is no reason to suppose that it could not develop as well after the intravenous or even the oral administration of calcium.

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8. Shannon, W. R.: Etiology of the Tetany Syndrome in the New Born, Arch. Pediat. **51**:23 (Jan.) 1934.

9. Albright, F., and Ellsworth, R.: Studies on the Physiology of the Parathyroid Glands: I. Calcium and Phosphorous Studies on a Case of Hypoparathyroidism, J. Clin. Investigation **7**:183 (June) 1929.

Such a possibility cannot fail to create a feeling of uncertainty as to the safest course to be followed in treatment for tetany of the newborn.

The suggestion is made that, at least for the patients with low calcium values, perhaps parathyroid extract offers the greatest theoretic security against the development of this complication.[10]

It is hoped that the 2 cases reported here will stimulate the interest of other observers in this condition so that an answer to the questions that it raises may be speedily forthcoming.

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10. Since this article was written, MacBryde reported on the use of dihydrotachysterol in the treatment of hypoparathyroid tetany. One is inclined to think from his report that this drug might find excellent use in certain cases of tetany of the newborn (MacBryde, C. M.: The Treatment of Hypoparathyroid Tetany with Dihydrotachysterol, J. A. M. A. **110**:767 [March 5] 1938).

FEEDING THE INFANT WITH CLEFT PALATE WITH THE AID OF A DENTAL PLATE

REPORT OF FIVE CASES

J. H. SILLMAN, D.D.S.
NEW YORK

The infant with a cleft palate presents a difficult feeding problem. The medicine dropper, the spoon and the Breck feeding method are those most frequently employed. These methods are tedious and in many instances cause a baby to become fatigued and undernourished. The use of a nipple with an apron attachment which partly closes the cleft has not proved satisfactory. Feeding the baby by gavage can be done only by a specially trained person.

I have a method whereby the baby with a cleft palate can be fed from a bottle and an ordinary nipple as quickly and as easily as the normal baby. This is accomplished with the aid of an accurately fitted dental plate which is inserted prior to each feeding. A version of this idea, basically the same, has been used abroad with success.[1]

The plate is made with a stone model obtained from an impression of the palate taken with modeling compound.[2] It is approximately 1/16 inch (0.16 cm.) thick. The surface in contact with the palate is made of soft vulcanite, while the other surface is made of hard vulcanite to give the necessary stiffness. (I have used latex and base plate gutta-percha as temporary materials.) The plate should rest only on the oral mucosa and should not come in contact with the nasal mucous membrane.

To assure the best results, the nipple should have three holes, each approximately the size of a 23 gage wire, so that the milk will flow readily as soon as the infant touches the nipple with his tongue. The milk is expressed by mechanical action and not by the act of suction, as only the hard palate is covered by the plate and, moreover, the infant cannot cup the nipple if a harelip is present. It is most important that

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Read before the Section of Pediatrics of the New York Academy of Medicine, March 10, 1938.

From the Department of Orthodontics, the Department of Obstetrics and the Department of Pediatrics of Bellevue Hospital.

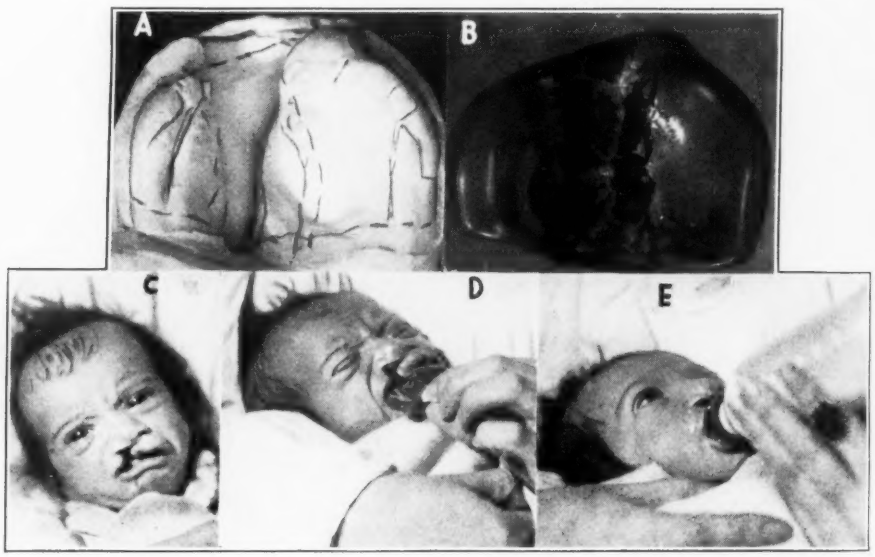
1. Fry, W. K.: The Dental Aspect of Treatment of Congenital Cleft Palates, Proc. Roy. Soc. Med. (Sect. Odontol.) **14**:57-68 (Oct.) 1921. Wearn, W. J.: The Immediate Dental Treatment of Cleft Palate Babies, Australian J. Dent. **34**:423-435 (Dec.) 1930.

2. Sillman, J. H.: The Relationship of the Maxillary and Mandibular Gum Pads in the Newborn Infant, Am. J. Orthodontics **24**:409-424 (May) 1938.

the same nurses be assigned for the feeding throughout the time the baby is hospitalized.

I have 5 cases to report in which infants with cleft palates were fed with the aid of an accurately fitted dental plate.

CASE 1.—Baby F., a boy, was spontaneously delivered at full term in the left occipitoanterior position, weighing 6 pounds 12 ounces (3,062 Gm.). He presented a complete unilateral cleft through the hard and soft palates, with a harelip on the right side, as seen in the accompanying illustration. The mother had congenital absence of some of the phalanges of the fingers. At 10 days of age the baby's weight was 6 pounds 8 ounces (2,948 Gm.). The mother fed him with a medicine



Photographs taken in case 1: *A*, cast of the palate; *B*, dental plate used as a feeding aid; *C*, the baby without the dental plate; *D*, the dental plate about to be inserted; *E*, nursing with the dental plate.

dropper, taking about an hour and twenty minutes for one feeding, and invariably the infant regurgitated part of his food. When awake he continually chewed his hands. On his twenty-second day (weight unknown) a dental plate was made and inserted before each feeding, thus enabling the infant to take his food from a bottle smoothly and steadily. After a few feedings the mother could give him 3 ounces (88 cc.) in about fifteen minutes. The mother also reported that since the baby had been fed in this manner the tendency to chew his hands had been greatly lessened. At 6½ weeks of age, this infant was admitted to Bellevue Hospital for surgical repair of the harelip. At this time his weight was 6 pounds 13 ounces (3,090 Gm.), which was only 1 ounce (28 Gm.) more than the birth weight. During the preoperative hospitalization period, of a month, the baby was fed with the aid of a plate, taking each feeding of 3½ ounces (99 cc.) in about seventeen minutes. He gained 19 ounces (539 Gm.) during this time. When the child was 11 weeks of age the plate made from an impression taken 9 weeks before was still being used with success.

CASE 2.—Baby M., a girl, was spontaneously delivered at full term, weighing 6 pounds (2,722 Gm.). She presented a complete cleft and harelip on the left side and a partial cleft on the right side. At first the infant was fed from a bottle with a nipple having a hole 3 mm. in diameter, through which the milk poured. The nurse would place the nipple on the intact portion of the infant's palate on the right side. While fed by this method the baby gained 21 ounces (595 Gm.) in five and a half weeks. Because an ulceration appeared on the palate, a dental plate was made. With this aid the infant nursed like a normal child and performed symmetric movements of the tongue and the jaws, which she had been unable to do without the plate. Within a week the ulceration improved and the infant gained 5 ounces (141 Gm.).

CASE 3.—Baby S., a girl, was spontaneously delivered prematurely, after twenty-nine weeks' gestation. She weighed 3 pounds 7 ounces (1,505 Gm.) and had a complete cleft through the hard and the soft palates and a harelip on the right side. The temperature ranged from 96 to 104 F., and this fever was accompanied by frequent convulsions of undetermined cause. After attempts to feed the infant by a medicine dropper had proved unsatisfactory, gavage was tried. Two months after birth, a dental plate was made, but this feeding aid did not prove successful. The infant would make a few suckling movements but then stop, and nothing could induce her to continue. I feel that the failure in this case was partially due to the poor condition of the baby.

CASE 4.—Baby U, a girl, was spontaneously delivered in the right occipito-anterior position at full term, after a normal, easy labor. She weighed 6 pounds 4 ounces (2,835 Gm.) at birth and was normal except for a complete cleft through the soft palate and a partial cleft of the hard palate. There was no harelip. The infant was fed with a medicine dropper and invariably regurgitated all or part of her food during feedings. She was discharged on the tenth day, weighing 5 pounds 8 ounces (2,495 Gm.), or 12 ounces (340 Gm.) less than the birth weight. Because the mother experienced great difficulty in feeding her, the baby was readmitted on the twenty-ninth day, weighing 5 pounds 14 ounces (2,665 Gm.). During the twenty-four days of her stay in the hospital the baby was fed with the aid of a dental plate and gained 12 ounces (340 Gm.). At the age of 18 weeks she weighed 10 pounds 5 ounces (4,678 Gm.). The same plate had been used for eleven and a half weeks.

CASE 5.—Baby D, a boy, was delivered at full term by version and breech extraction and weighed 7 pounds 4½ ounces (3,303 Gm.). The baby was born with a double harelip, a complete cleft of the hard and the soft palate on the left side and a partial cleft of the hard palate on the right side. An impression was taken on the first day, and two days later this baby was being fed successfully with the aid of a dental plate, taking 3 ounces (88 cc.) of his mother's milk from a bottle. After a few feedings he was taking his bottle in twenty minutes.

It is interesting to contrast the last 2 cases, as both of the babies came from the same nursery. The infant in case 4 had only a partial cleft of the hard palate and no harelip, yet on the tenth day she was 12 ounces (340 Gm.) under her birth weight. No dental plate was used during this period. On the other hand, the infant in case 5 had a double harelip, a complete cleft of the hard and soft palates on the left side and a partial cleft of the hard palate on the right side. He nursed with the aid of a dental plate from his third day and was up to his birth

weight on his fourteenth day. This difference illustrates the advisability of making the plate as soon after birth as possible.

SUMMARY

A method of feeding with the aid of an accurately fitted dental plate enables babies with cleft palates to be fed from a bottle like normal infants. Five cases are presented, in 1 of which the method was a failure. In no case did injury or irritation of the mucosa result from the use of the plate.

It is hoped that this appliance will solve some of the problems of feeding infants with cleft palate and will minimize the diseases of the respiratory tract to which these infants, partially because of the aspiration of fluids, are particularly susceptible. The infants will be given the opportunity to exercise their inherent urge to suckle, which will stimulate growth and development; this, in turn, may reduce the number of operative failures.

Dr. Charles Hendee Smith, Dr. William E. Studdiford and Dr. Leo Winter permitted me to carry out this work in their departments, and Dr. Harold S. Vaughan, Dr. Ruth Bakwin and Dr. Harry Greenwald allowed me to include their patients in this report.

TREATMENT OF PERITONEAL SYNDROME AND ERYSIPELAS-LIKE LESIONS OF SKIN IN NEPHROSIS

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Complications of nephrosis have been described since early in the history of the disease. This report deals only with clinical observations on and attempts at treatment of two of these complications, the peritoneal syndrome and erysipelas-like lesions of the skin.

The association of pneumococcic peritonitis with nephrosis was first recorded by Volhard and Fahr,[1] in 1914, when they reported 3 such cases. Volhard[2] added 3 more case reports in 1918. Munk[3] also reported a case in 1918. Bock and Mayer[4] described another in 1920, and thereafter the reports became more frequent. Mortality rates were not discussed in these earlier reports, but practically all cases of peritonitis were described from postmortem rather than from clinical observations. Stewart[5] in 1930 collected from the literature case reports of 23 patients, 21 of whom died. In all cases the diagnosis was proved by culture. He added case reports of 3 patients of Dr. E. A. Park, all of whom survived their attacks of peritonitis and were living at the time of publication of the report. In two of these cases the diagnosis was proved by culture, and in 1 it was not. However, most writers have agreed that the presence of pneumococcic peritonitis speaks for an extremely grave prognosis. No discussions of treatment for this condition have been found; Stewart mentioned surgical drainage but did not advise it.

From the Nephritic Clinic of the Children's Memorial Hospital.

1. Volhard, F. and Fahr, T.: Die Brightsche Nierenkrankheit: Klinik, Pathologie und Atlas, Berlin, Julius Springer, 1914.

2. Volhard, F.: Die doppelseitigen hämatogenen Nierenerkrankungen (Brightsche Krankheit), Berlin, Julius Springer, 1918.

3. Munk, F.: Pathologie und Klinik der Nierenerkrankungen (Nephrosen, Nephritiden und Schrumpfnieren), ed. 2, Berlin, Urban & Schwarzenberg, 1925.

4. Bock, G., and Mayer, E.: Ein Fall von genuiner Nephrose mit Pneumokokken-peritonitis als Ausgang, Med. Klin. **16**:101 (Jan. 25) 1920.

5. Stewart, W. B.: The Pneumococcus in Nephrosis, J. M. Soc. New Jersey **27**:21 (Jan.) 1930.

Erysipelas-like lesions of the skin occur less frequently than peritonitis as a complication of nephrosis, and little discussion of them has been found in the literature. Erysipelas was mentioned occasionally in earlier reports, and Schwarz and Kohn [6] mentioned it in 1922 but did not describe any cases. In view of later observations, it is believed that true erysipelas is a rare complication but that lesions similar to the eruption of erysipelas are much more frequently present. Keefer and Yang [7] have given an excellent description of this condition and have reported 7 cases, the patients being chiefly young adults. The onset and course, as they described them, were practically identical with those observed by us in children. Since this condition is not widely recognized or described, the following paragraph is quoted from their report:

> A patient with the typical signs of nephrosis suddenly develops fever, chilliness, and in some instances abdominal pain, nausea and vomiting. . . . Soon after the onset of fever, the patient usually complains of pain in the back, and it is particularly noticeable in the lumbar region. When the painful area is examined, no objective changes may be observed. Within twelve to twenty-four hours after the onset there is exquisite tenderness over the painful area with signs of acute inflammation of the edematous skin and subcutaneous tissues. The skin is red and the local temperature increased. The erythematous area varies in size, and in the beginning it may not be more than two or three centimeters in diameter. The edges are not raised and the tenderness extends over a greater area than the redness. This inflammation spreads peripherally with amazing rapidity and it is difficullt for the patient to find a comfortable position in bed on account of the pain and tenderness. It is characteristic for the inflammation to spread and migrate into the most dependent parts.

One of their patients had pneumococcic peritonitis, the diagnosis being proved by culture. At autopsy, sections of the lower part of the abdominal wall contained gram-positive diplococci. One patient had a localized pneumococcic abscess, and another had pneumococcic pneumonia; the diagnosis in both cases was proved by culture. The authors specifically mentioned that in 4 cases the edematous fluid from the affected areas of the skin was sterile.

Keefer and Yang made another observation which agrees with ours: that the cutaneous lesions occurred on the lower part of the trunk, the lower extremities and the genitalia but never higher. The chief difference between their observations and ours is the fact that the peritoneal syndrome was observed in practically all of our children who had erysipelas-like lesions of the skin. In 6 of their 7 patients the lesions occurred without symptoms of peritonitis; there was only 1 such instance among our patients. The authors gave no discussion of treatment.

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6. Schwarz, H., and Kohn, J. L.: Studies of Nephritis in Children: I. Nephrosis, Am. J. Dis. Child. **24**:125 (Aug.) 1922.

7. Keefer, C. S., and Yang, C. S.: Erysipeloid Skin Rashes Complicating Nephrosis, Nat. M. J. China **16**:524 (Oct.) 1930.

Other complications of nephrosis which have been recorded are subcutaneous abscesses, infections of the upper respiratory tract, pneumonia and septicemia. We have observed these, but they are not reported here in detail. We have not observed an unusually marked incidence of disease of the accessory nasal sinuses, which has been reported by some. Recently asthmatic bronchitis has been noted frequently in our children with nephrosis.

REPORT OF A CASE

In July 1934 J. F., a 2½ year old boy, entered the Children's Memorial Hospital with massive edema and the typical history and findings of nephrosis. He had no fever at the time. Six days after the child's admission the temperature rose to 105 F. and abdominal pain and tenderness with vomiting developed. Simultaneously the skin over the lower part of the abdomen on both sides became red and warm. This area was exquisitely tender. The inflammation spread rapidly toward the groins. Because of the resemblance of the cutaneous lesion to the eruption of erysipelas (although the condition was not considered true erysipelas) one of us (C. A. A.) suggested the use of convalescent serum. On the next day 100 cc. of human erysipelas convalescent serum was given intramuscularly. There was immediate improvement, not only in the cutaneous condition but in the abdominal symptoms and findings. After three days the temperature was normal and the boy was much improved.

MATERIAL AND METHODS

After the good resullts in the case just described, the use of convalescent serum was instituted as routine treatment when the peritoneal syndrome appeared with or without cutaneous lesions. At first erysipelas serum was used, but because we were not able to procure this later, convalescent scarlet fever serum was used instead. In all cases in which it was possiblle to use a vein the serum was given intravenously. No untoward reactions were noted. The amount used was from 60 to 100 cc., if that quantity could be procured.

Cultures of the peritoneal fluid or of the edema fluid from affected areas of the skin were not made in most of these cases. Symptoms of peritonitis develop so rapidly that it was not considered wise to withhold a treatment which offered so much hope while waiting for a report on a culture. We felt, moreover, that the action of the serum could not be due to specific antigenic properties, as we obtained several cures by crisis even when the infection was known to be pneumococcic. Pneumococci were cultured from the peritoneal fluid, obtained at autopsy, of 4 patients in this series, and staphylococci were obtained from the fluid of 1. In 2 instances there was no growth from cultures of the ascitic fluid taken at the onset of symptoms, a frequent finding even with proved pneumococcic peritonitis.

We use the term peritoneal syndrome because it has been repeatedly pointed out that pneumococcic peritonitis cannot be proved to exist in the living patient without culture of the peritoneal fluid. On the other hand, it was the clinical judgment of various associated attending physicians, interns, residents and the chief of staff, Dr. Joseph Brennemann, as well as our opinion, that these patients actually suffered from peritonitis.

TABLE 1.—*Summary of Cases in Which Serum Was Used*

Case No.	Patient	Age (Yr.)	Complication	Serum: Dose, Cc.	Serum: Type*	Results
1	G. B. (2 attacks)	11	Peritoneal syndrome	100	s.f.	Temperature fell from 102.6 F. to normal in 2 days; loss of 14 lb. in 7 days
		11	Peritoneal syndrome	100	s.f.	Temperature fell from 103.4 F. to normal in 3 days; loss of 10 lb. in 7 days
2	J. C. (5 attacks)	3	Peritoneal syndrome	100	s.f.	Temperature fell from 103.5 F. to normal in 2 days
		3	Peritoneal syndrome; erysipelas-like lesions	100	s.f.	Temperature remained high because of abscesses in thigh, but abdominal symptoms subsided next day
		3	Peritoneal syndrome	60	s.f.	Temperature fell from 105 F. to normal in 2 days
		3	Peritoneal syndrome; cellulitis of thigh	100	s.f.	Temperature fell from 103 F. to normal in 3 days; loss of 4 lb. in 4 days
		4	Peritoneal syndrome; pneumonia	100	s.f.	No effect; patient died during attack
3	H. F. (2 attacks)	7	Peritoneal syndrome; erysipelas-like lesions	60	s.f.	Temperature fell from 102 F. to normal in 2 days
		7	Peritoneal syndrome; pneumonia	60	s.f.	No effect; patient died during attack
4	J. F. (5 attacks)	2½	Peritoneal syndrome; erysipelas-like lesions	100	ery.	Temperature fell from 105 F. to normal in 3 days
		5	Peritoneal syndrome	60	s.f.	Temperature fell from 101 F. to normal in 2 days
		5	Peritoneal syndrome	80	s.f.	Temperature fell from 103 F. to normal in 5 days; loss of 6 lb. in 4 days
		5	Peritoneal syndrome	80	s.f.	No effect
		5	Peritoneal syndrome; pneumonia; septicemia	100‡	s.f.	No effect; patient died during attack
5	T. H. (2 attacks)	5	Peritoneal syndrome	100	s.f.	Temperature fell from 104.4 F. to normal in 6 days; loss of 18 lb. in 7 days
		5	Peritoneal syndrome	100	s.f.	No effect; patient died during attack
6	F. K.	1½	Peritoneal syndrome	80	s.f.	Temperature fell from 103 F. to normal in 4 days; loss of 5 lb. in 10 days
7	A. K.	10	Peritoneal syndrome; erysipelas-like lesions	100	ery.	Temperature fell from 102.8 F. to normal in 2 days; gradual loss of 12 lb. during next 3 weeks
8	E. K.	11	Peritoneal syndrome	100	ery.	No effect; patient died during attack
9	F. M.	5	Peritoneal syndrome; erysipelas-like lesions	60	s.f.	Temperature fell from 101.5 F. to normal in 2 days
10	N. S.	4½	Peritoneal syndrome	40	ery.	Temperature normal when serum was given; it remained normal, and symptoms of peritoneal syndrome subsided next day
11	N. T.	3	Peritoneal syndrome	100	s.f.	Temperature fell from 100.5 F. to normal in 2 days
12	J. W.	3½	Erysipelas-like lesions	40 10	ery. s.f.	Temperature fell from 103 F. to normal in 4 days

* "s.f." indicates scarlet fever convalescent serum; "ery." erysipelas convalescent serum.
‡ This injection was given 2 days after the preceding one.

Perhaps our reluctance to perform intraperitoneal taps is unjustified, but it resulted from two or three instances in which we attributed peritonitis to previous abdominal paracenteses. Moreover, it must be remembered that in many instances the presence of erysipelas-like cutaneous lesions over the lower part of the abdomen made us hesitate to go through this infected skin into the peritoneal cavity. Finally, whenever patients whose condition was diagnosed as peritonitis were examined at autopsy, we were able to demonstrate this disease. There are records of 10 such instances in our hospital files. When a child with nephrosis becomes critically ill with vomiting preceded by a few loose stools and followed by high fever, leukocytosis, rapid pulse and generalized tenderness, rigidity and pain over the abdomen, the picture is alarming to any one experienced in dealing with nephrosis. It is this syndrome, whether or not it is due to true peritonitis, which we have attempted to treat.

There was no question as to the diagnosis of the erysipelas-like lesions of the skin, as they were visible. Bacteriologic studies of the skin were not made in our cases. In the few cases reported by Keefer and Yang the cultures were negative.

TABLE 2.—*Summary of Results of Treatment*

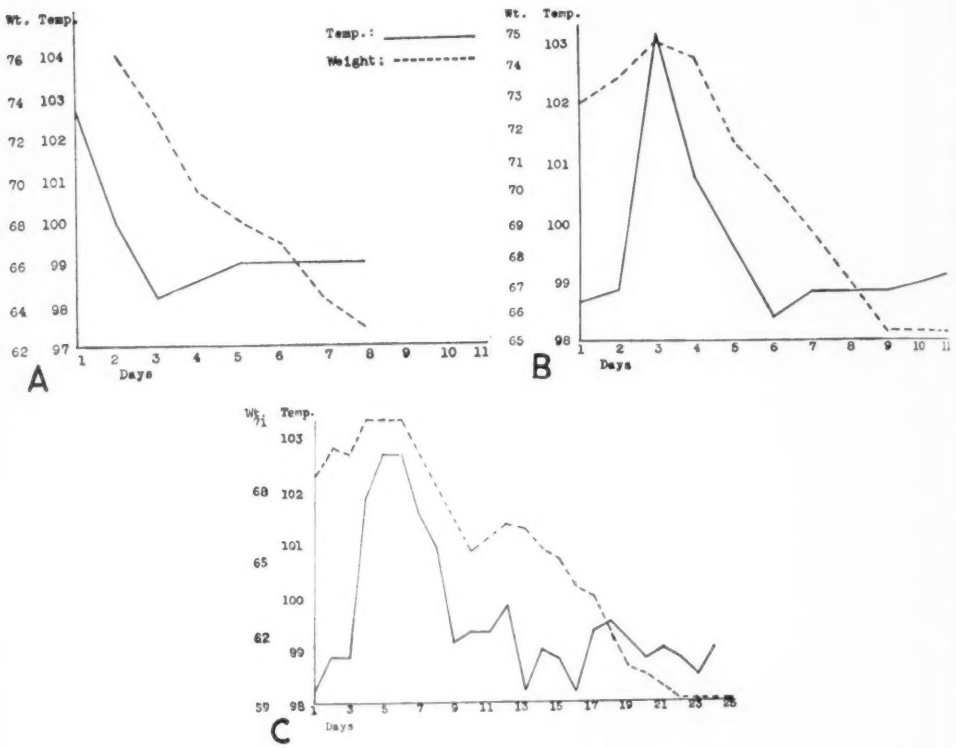
Result	No. of Attacks
Temperature	
Prompt reduction	15
No effect	8
Weight	
Prompt diuresis with loss of weight	7
No record because patient was too ill to weigh	4
No effect	12
Clinical course	
Prompt recovery from attack	17
No effect	6
Patient died during attack	5

Control cases were not used because we did not feel justified in withholding the treatment from those who became ill. However, in looking over our previous records we found 3 instances of erysipelas-like cutaneous lesions, in 2 of which the eruption was accompanied by fatal pneumonia. Cultures were not made. The other patient had subcutaneous abscesses which contained Streptococcus viridans. Three other children had the peritoneal syndrome; 1 survived and 2 died. Autopsy revealed purulent peritonitis in 1. No cultures were made of material from any of the patients in this early group. While it is well known that children occasionally survive, it is equally true that the prognosis of the peritoneal syndrome is grave, as the disease has a mortality of at least 2 deaths in 3 cases.

RESULTS

Table 1 includes a list of the children for whom the treatment was used, with their ages and the number of attacks. The type of complication present, the kind and amount of serum used and the effects on temperature and weight are also given. In cases in which results were favorable the temperature and clinical symptoms abated with startling rapidity. We do not place too much emphasis on the losses of weight in some of the patients because all who have observed nephrosis know

that diuresis may follow any febrile infection or may occur spontaneously without apparent reason. A summary of the effects on temperature, weight and clinical symptoms is given in table 2. It should be pointed out that the low grade of temperature reported in some of these patients was due to extremely early treatment, as we have felt it advantageous to attempt to abort the attack rather than to allow it to develop to its full extent.



Results of treatment in 3 cases. *A* represents the temperature and weight during the first attack of G. B. (case 1), who entered the hospital during the attack. Serum was given on the first day. *B* shows the second attack of the same patient. Serum was given on the third day. *C* indicates the temperature and weight of A. K. (case 7), who was given serum on the fifth day.

The chart shows the results in 3 specific cases.

COMMENT

In our clinic the immediate mortality from the peritoneal syndrome complicating nephrosis has been decidedly reduced, only 5 fatalities occurring in 22 attacks. Among previous patients afflicted with the disease who were not so treated, 2 of 3 children died.

The question which naturally arises is why patients presumed to have a pneumococcic infection should respond favorably to convalescent serum from patients with streptococcic infections. Two possible reasons come to mind. One is that convalescent serums have long been known to have nonspecific beneficial effects in patients with various diseases. This has been part of the rationale back of much of the current enthusiasm for transfusions. Study of the temperature curves in many cases shows a crisis-like response not at all like the gradual improvement seen in spontaneous recovery. The second possibility is that the intravenous injection of this amount of normal serum may influence the nephrotic element favorably and thus put the patient in better condition to fight the peritoneal or the cutaneous infection.

It is apparent from table 1 that all patients with the erysipelas-like lesions promptly recovered after the serum treatment whether or not the peritoneal syndrome was present. This fact may be of some importance in making a prognosis when both complications occur. It should also be pointed out that the most serious prognosis is encountered in those cases in which the patients have definite septicemia.

SUMMARY

An apparent reduction in mortality from the peritoneal syndrome complicating nephrosis was observed in patients treated with large doses of either erysipelas or scarlet fever convalescent serum.

In this series there were but 5 deaths in 22 attacks of the peritoneal syndrome.

All of the patients who had the erysipelas-like cutaneous lesions recovered promptly after serum treatment.

Two possible reasons for these results are briefly discussed.

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Case Reports

DUODENAL OCCLUSION IN THE NEWBORN

SUCCESSFUL OPERATION ON A PREMATURE TWIN

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In a survey of the literature on the subject of intestinal obstruction, one is struck by the looseness and inaccuracy of the terms used to describe the various conditions encountered.

The words obstruction, occlusion, atresia, stenosis and aplasia are often interchanged, which confuses the reader as well as distorts the meaning of the writer. For this reason an explanation of the terms as used here is indicated.

By obstruction is meant any blocking or clogging of the lumen of the intestine which hinders the passage of intestinal contents. An occlusion is a complete closure of the lumen of the intestine; it is commonly referred to as a complete obstruction. Atresia, as its Greek derivation (*α-τρητος* without a boring) implies, is an imperforation, an absence or a closure of the intestinal lumen. The word has been used by many in this strict sense, but to most it signifies not only the occlusion of the bowel from some intrinsic congenital error of development but any degree of constriction or narrowing of the lumen due to some developmental defect of one or all of the intestinal coats—it includes both occlusion and stenosis. Atresia presupposes the existence, at some time in the development of the bowel, of a lumen, of which there is subsequently complete (occlusion) or partial (stenosis) obliteration. In such a comprehensive sense is it used here. Aplasia, on the other hand, is the absence of the development of a lumen, i. e., a condition in which presumably a lumen never did exist and in which frequently even the mesentery is absent.

Duodenal obstruction in the newborn is congenital or acquired.

The acquired type is either (*a*) mechanical and caused by such fetal accidents as hernia, volvulus, Meckel's diverticulum, bands and

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From the surgical service of De Witt Stetten, M.D., Lenox Hill Hospital.

Read before the Surgical Section of the New York Academy of Medicine, Dec. 3, 1937.

infection, or (*b*) adynamic and neuromuscular in character and much the same in origin as Hirschsprung's disease is thought to be.

The etiology of the congenital forms is still far from clear and remains theoretic. Meckel, Balfour, Tandler, Kreuter, Cautley and Albers felt that it is due to the failure of the bowel to acquire a lumen during embryonic life. Filimowski, Schridde, Johnson, MacCallum, Simpson and Weber expressed the opinion that the lumen was obliterated in the course of development by epithelial proliferation. Fiedler, Savariaud, Theremin and Mauclaire and Alglave stated that they considered these occlusions as inflammatory, while others have ascribed them to changes in the vascular systems of the intestine (Jaboulay, Küttner, Durante, Wyss, Taillens, Davis and Poynter).

The mechanical type, according to Mohrmann, Mikulicz and Kausch, Serr, Gaertner, Brun and Chiari, is explained by extrinsic causes, such as herniation, pressure of the head of the pancreas and intussusception.

The adynamic type is probably due to a defect in the neuromuscular system of the intestine (Okinczyc, Hartman, Treves, Grisel, Kirmisson).

Cordes, in 1901, and Spriggs in 1912, contributed excellent reviews of congenital intestinal obstruction. Their conclusions as to the end result of any form of treatment were discouraging indeed. They considered the prognosis hopeless because up to that time not a single patient had survived any form of treatment, and the many forms of surgical intervention attempted had all proved fatal. Webb and Wangensteen, in a thorough paper published in 1931, sounded a much more encouraging note, in that they found reported in the literature 9 cases of intestinal obstruction in newborn infants who were successfully operated on. In 5 of these there was occlusion at some part of the duodenum; they are reviewed briefly here.

In 1916 Ernst reported a case of obstruction caused by duodenal atresia in an 11 day old infant, on whom he performed a successful duodenojejunostomy.

In the same year Weeks and Delprat relieved congenital occlusion of the third portion of the duodenum in a 6 day old infant by means of a gastroenterostomy. The occlusion was produced by atresia of the third portion of the duodenum behind the mesenteric attachment.

Richter in 1924 had a similar case in a 4 day old infant whose intestine was obstructed by duodenojejunal atresia; a gastroenterostomy was successful in this case also. In the same year Cutler in a personal communication to Loitman stated that he had successfully performed a gastroenterostomy in a 4 day old baby with duodenal obstruction from atresia.

The following year (1925) Bolling performed a duodenojejunostomy on a 5 pound (2,268 Gm.) baby on the ninth day after birth. This infant had vomited from the first nursing and had had frequent

typical meconium stools. At operation the stomach and duodenum were markedly dilated, and the jejunum was collapsed. No attempt was made to ascertain the cause of the obstruction. The convalescence was stormy for several days and was complicated by infection of the wound. When discharged from the hospital the child was free from symptoms and was gradually gaining weight.

In 1927 Steward, and later Sweet and Robertson, had 2 cases attended by a happy result. Steward's case was not reported; it was only mentioned in a discussion of MacLennan's paper by Cameron, who stated that the procedure was a gastroenterostomy for duodenal atresia. In Sweet and Robertson's case a gastroenterostomy was done on the ninth day after birth; twelve days later this was supplemented by a duodenojejunostomy to relieve the vomiting which had continued after the first operation. The end result was excellent.

In 1933 Carter contributed a case in which the condition was produced by a thick band running between the hepatic flexure of the colon and the gallbladder, the band compressing the duodenum just below the pylorus. The operation consisted in severing the peritoneal band.

In 1935 Donovan encountered 2 cases of duodenal obstruction at the point where the superior mesenteric vessels passed over the duodenum. The infants were 9 and 17 days old, respectively, and had vomited consistently since birth. The stools were regular and consisted mostly of meconium. Both were relieved by duodenojejunostomy anterior to the colon.

To these should be added my case:

REPORT OF A CASE

D. R. was one of twin girls delivered by cesarean section on July 18, 1937. Both babies were born after about eight months' gestation. The weight at birth was 4 pounds and 6 ounces (1,984 Gm.). The child took about 4½ ounces (132 cc.) of fluid on each of the first two days. On the third day she took her feeding poorly, and on the fourth day she vomited most of her feeding. At this time she was admitted to the pediatric service of Dr. Jerome Leopold. A starvation period of six hours was instituted, and the baby was fed frequently small amounts. Everything proceeded nicely for the next six hours, but then the vomiting recurred. During this period the fluid intake was maintained by clysis.

Up to this time the stools consisted only of meconium, as contrasted directly with those of the smaller twin sister, who was already having normal bowel movements.

Physical examination revealed a restless infant of about 4 pounds (1,814 Gm.) with knees drawn up, crying spasmodically. The abdominal veins were prominent, and the abdomen was distended but not rigid. No visible peristalsis was observed. Rectal examination was negative. The provisional diagnosis was high congenital intestinal obstruction.

A barium sulfate clysma was given first; it was followed by a small thin barium sulfate meal given by mouth. The barium sulfate enema revealed no obstruction in the colon. Roentgen examination of the stomach showed complete retention at the end of five hours. The temperature was 103 F., and the pulse rate was too rapid to count. The infant appeared to be moribund, and it was with great reluctance that surgical intervention was undertaken.

Laparotomy was performed about five hours after completion of roentgen studies, with the patient under open drop ether anesthesia. An upper right rectus incision was made, extending from the costal margin to below the umbilicus.

The stomach and the proximal 1 inch (2.5 cm.) of duodenum were markedly distended. The walls of the stomach seemed somewhat thickened in spite of the distention. The duodenum at the point of obstruction, which was about 1 inch

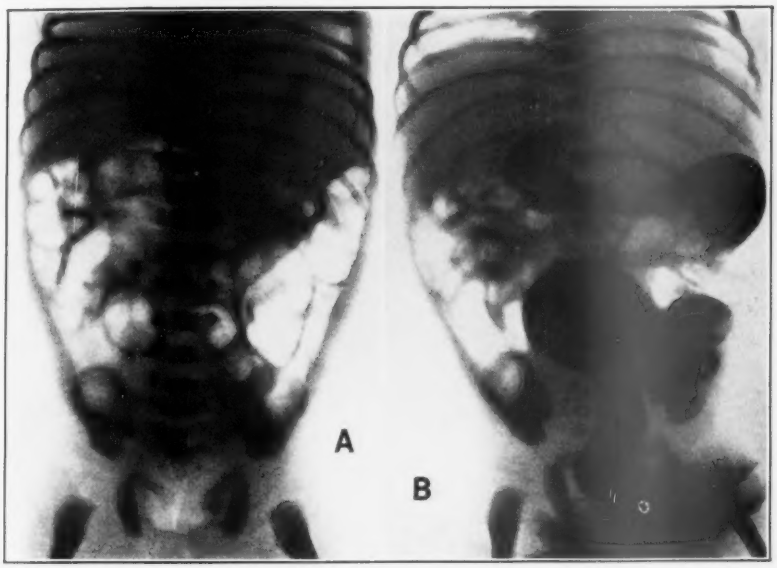

Fig. 1.—*A*, flat plate showing distention of intestine; because of this distention it is impossible to localize the obstruction. *B*, the plate taken after administration of a barium sulfate enema, reveals good filling of the colon throughout.

below the dilated pylorus, was kinked and fixed by a wide peritoneal band to the under surface of the liver, medial to the gallbladder, at the level of the cystic duct. The band issued from the posterior surface of the duodenum and ran over it to become attached to the liver. The duodenum below the occlusion was not ribbon-like but rather cordlike and so tough that the presence of a lumen could not be definitely ascertained by palpation. At the duodenojejunal angle the intestine was collapsed and ribbon-like, as with intestinal obstruction. The picture at this time was that of a kinking of the duodenum with atresia (fig. 3).

Procedure.—The intestines were retracted by the assistant's hand to obviate the shock of gauze packing. An incision was cautiously carried through the peritoneal band, and a bluish structure was seen to pout through. This was identified as the portal vein. When the incision was carried a little farther to

the right, the common duct came into view. When this was traced down for about 0.5 cm., it was seen that it became so intimately associated with the duodenum that they seemed to merge. At this stage it looked as if the kink were due to shortness of the common duct as well (fig. 4).

The patient's condition was so poor by this time that a gastroenterostomy, which was considered the procedure of choice, would undoubtedly have proved fatal. The duodenum was mobilized sufficiently to straighten the kink, the intention being to maintain this position by suturing it to the surface of the liver, in the hope that the duodenum would prove to be patent.

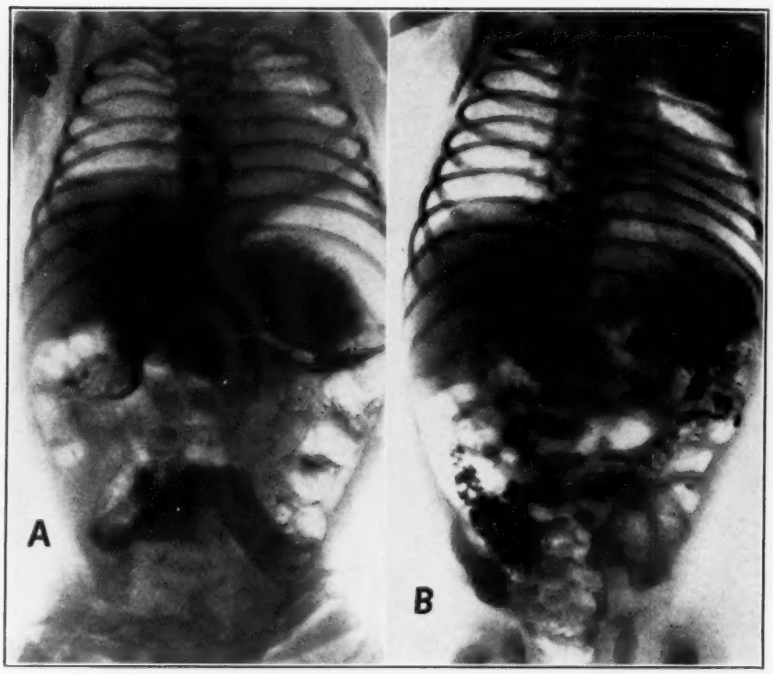

Fig. 2.—*A*, the plate taken after a thin barium sulfate meal was given, reveals the stomach to be distended with gas and obstructed at the pylorus, as evidenced by retention of the barium sulfate. The barium sulfate seen in the colon is residual from the clysma given immediately before the meal. *B*, was taken five hours after the barium sulfate meal was given. The diminished quantity of barium sulfate in the stomach as compared with that shown in the immediate roentgenogram is due to the frequent vomiting which occurred between roentgen exposures. Residual barium sulfate from the clysma is seen in the colon. No barium sulfate has penetrated the duodenum, which indicates obstruction at the first portion.

While this was being done the common duct was seen to pass behind the duodenum and turn on itself to enter its distal surface, being adherent throughout. The mobilization of the duodenum was then abandoned, and an attempt was made to peel the duodenum off the common duct and portal vein. While this procedure was being executed the portal vein was nicked slightly; the hemorrhage was controlled by a gauze tampon, which was left in situ and not removed until

four days later. This maneuver straightened out the kink but did not relieve the obstruction. Again it was felt that the condition was atresia. On close inspection, however, one observed that the same band that had kinked the duodenum had produced a twist in the longitudinal axis because it took origin on the posterior surface of, and ran over, the intestine to become adherent to the liver (fig. 2). As soon as this was recognized, the duodenum was mobilized for about 2 inches (5 cm.) more. The volvulus was then straightened out, which allowed the contents of the stomach to pass through with an audible gurgle, and the seemingly

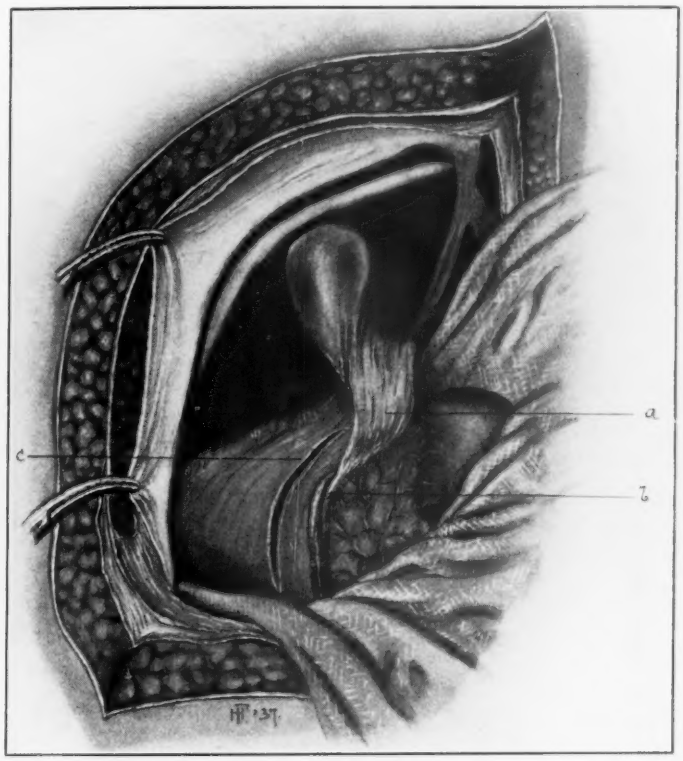

Fig. 3.—The condition found at operation; *a* indicates the band of adhesions; *b*, the collapsed and twisted duodenum (volvulus), and *c*, the incision in the posterior part of the peritoneum. The first portion of the duodenum is shown fixed to the under surface of the liver by a wide peritoneal band, which produces an acute kinking of the duodenum just below the pylorus. It was felt that the severance of the band would relieve the obstruction. This was only partly cut through when a bluish structure (the portal vein) pouted through the incision. As the band was pulled forward, the common duct was identified just to the right of the portal vein.

atretic duodenum ballooned out nicely throughout its whole length. The remainder of the intestinal tract was inspected, but no other abnormality was found.

The infant went into surgical shock several times during the operation. This was attributed to the handling of the intestines. At these times the procedure

was stopped, the wound was covered with a moist laparotomy pad, and a couple of minutes were allowed to elapse to relieve shock before the operation was resumed. The respite thus provided probably played an important role in the patient's recovery.

Shortly after the closure of the peritoneal cavity the condition of the patient changed for the better, and she was returned to the incubator. During the immediate postoperative course, oxygen and carbon dioxide were administered to maintain respiration. Two transfusions were given; the first, one-half hour after the operation, and the other, the following morning. In both cases 50 cc. of citrated blood was given, the donor being the father.

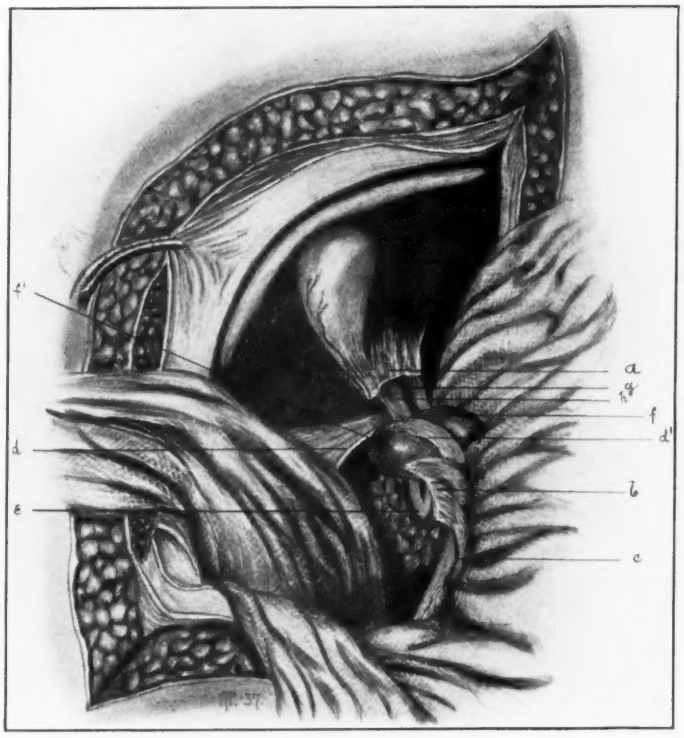

Fig. 4.—The condition at a later stage of the operation; *a* indicates the proximal cut end of the peritoneal band; *b*, the distal cut end of the peritoneal band; *c*, the collapsed and twisted duodenum (volvulus); *d*, the proximal edge of the incised posterior part of the peritoneum; *d'*, the distal edge of the incised posterior part of the peritoneum; *e*, the common duct, turning on itself to enter the duodenum; *ff'*, the dilated portion of the duodenum above the volvulus; *g*, the portal vein, and *h*, the common duct. An incision was then carried through the peritoneum in order to mobilize the duodenum so as to straighten out the kink and, if necessary, to hook up the duodenum to the under surface of the liver to prevent future kinking. During this procedure it was discovered that the common duct was not short but rather passed behind the duodenum and turned on itself to enter the duodenum in its distal surface. The pull of the band attached to the distal surface of the duodenum produced a twist in its longitudinal axis, causing a volvulus.

There was some oozing from the lower third of the incision but not from the packing at the upper angle of the wound which was used to control the bleeding from the injury to the portal vein.

Within two hours of the operation the child began to take fluid by mouth, without any vomiting; this was well tolerated. On the second postoperative day she began passing barium sulfate in the stool, and later the stool became soft, yellow and pasty.

The wound healed well, and the packing was removed on the fourth day. No vomiting occurred at any time after the operation. The child continued to take feedings well and began to gain weight. The formula was increased in both strength and quantity. The remainder of the convalescence was uneventful. The baby was discharged on the thirtieth postoperative day, thirty-four days after birth. Four months later the child weighed 12 pounds and 13 ounces (5,812 Gm.), and a check up on the gastrointestinal condition by a series of roentgen studies revealed perfect function.

Carter, including his own case and using Webb and Wangensteen's statistics as a basis, brought the number of successful operations of intestinal obstruction in the newborn up to 11.

Strictly considered, 1 of the cases included in Webb and Wangensteen's series is not relevant and is excluded here: This is Abel's case (quoted by Loitman), in which a gastroenterostomy was performed for definite hypertrophic pyloric stenosis, now so readily cured by the method of Ramstedt. The case, however, did serve to demonstrate the feasibility of a gastroenterostomy in an extremely young infant.

To the present time, as far as I could ascertain, the reported successful operations for intestinal obstructions in the newborn are those of Ernst, Weeks and Delprat, Richter, Cutler, Bolling, Steward, Sweet and Robertson, Carter, Donovan (2 cases) and Stenson for duodenal obstruction (11 cases) and those of Fockens, Demmer, Carter and Davenport and Goldberg for intestinal obstruction below the duodenum (4 cases).

In all of these cases the cardinal symptom was vomiting, which was present in all cases reviewed except those of 2 patients who died without having vomited.

In the vast majority there was some impairment of intestinal action to a degree ranging from complete absence of stool to the passing of meconium which varied only in amount and appearance. The meconium in some was reported as being deeply bile stained and in others just slightly so, according to whether the obstruction was above or below the junction of the common duct with the duodenum. Many cases are reported, however, in which the obstruction, apparently complete and verified by autopsy, was either above or below the entrance of the common duct into the duodenum, producing the phenomenon of bile-stained vomitus or bile-stained meconium, respectively. How the bile

reached a region above or below the obstruction is still a matter of conjecture. An aberrant bile duct may explain the phenomenon in some cases but certainly not in all of them.

Considerable distention is a common sign; it varies to some extent with the site of obstruction. The difference between the distention of a high and that of a low obstruction is not great enough in most cases to localize the lesion, except in the few instances in which visible peristalsis is present.

The diagnosis, generally obvious, should be confirmed by roentgen study, which is also the only practical way of localizing the lesion. A solution of thin barium sulfate should be used to lessen the possibility of completing the obstruction or of producing impaction. It is safer to give a barium sulfate enema first; if sufficient information is not obtained, this should be followed by a small thin opaque meal.

Infants suffering from this condition not only look very sick but are extremely ill and present to the surgeon anything but an encouraging outlook. However, if he does not come to the rescue they are irrevocably doomed to die, and the problem should be tackled with full recognition of this fact.

When one considers that in the large necropsy service at Bellevue Hospital, St. George encountered only 2 cases in fourteen years, that Theremin reported finding only 9 cases in reports of 150,000 autopsies in St. Petersburg and 2 in reports of 111,000 autopsies in Vienna, that Ernst found 2 in 41,000 autopsy reports in Copenhagen and that Farr and Fries estimated its occurrence at 1 in 20,000 newborn infants, the impression is created that these cases are extremely rare.

On the other hand, a study of the literature, which reveals several hundred reported cases in which there were only 15 recoveries, leads one to think that these fatalities are too numerous and could be materially reduced by timely and appropriate surgical intervention.

The procedure most commonly done is some form of enterostomy or side-tracking operation. In all reported instances of enterostomy, which are now numbered in the hundreds, the termination was fatal. For some reason newborn infants do not stand this procedure. Gastroenterostomy, duodenojejunostomy, enteroenterostomy and ileocolostomy are better tolerated and are the safest procedures when they are strictly indicated. They present, however, considerable technical difficulty, which arises more from the contraction of disuse of the obstructed loop than from its collapse. This contraction often narrows the lumen to such a degree as to render an anastomosis impossible unless the narrowed lumen is distended with fluid or air is injected into it. This contraction of disuse may be so marked that its differentiation from atresia is practically impossible. It presents the wormlike or cordlike appear-

ance which is so commonly referred to as characteristic of atresia and which is very different from the ribbon-like appearance of a simple collapse usually produced by obstruction. In the case reported here, had not the lumen ballooned out under pressure from the contents of the stomach, the condition would have been considered atresia because there is no way of definitely identifying atretic stenosis without opening the lumen.

Even at autopsy, in cases of multiple areas of atresia, the contraction of the intestine between the stenosed areas is often difficult to distinguish from the stenosis itself, so pronounced is it. Since an enteroenterostomy is difficult and serious in a newborn infant even under the most favorable conditions, it is wise to make sure that this procedure is the only way out.

SUMMARY

Although congenital intestinal obstruction in the newborn is rare, many hundreds of cases have been reported from autopsy records. The 14 reported cases in which the condition was cured by surgical means are briefly reviewed in the present study, and 1 of my own is reported in greater detail.

CONCLUSIONS

1. Congenital intestinal obstruction in infants is rare but too frequent to be negligible.

2. Vomiting is the principal symptom. Impairment or cessation of intestinal action is the principal sign.

3. Administration of a barium sulfate enema followed if necessary by a thin barium sulfate meal is the best means of confirming the diagnosis and localizing the lesion.

4. The critical physical condition of the infant is no contraindication to operation.

5. The contraction of disuse may simulate atresia.

6. For atresia the operation of choice is an anastomosis. The injection of air or fluid into the collapsed bowel facilitates the operation.

7. Enterostomy is fatal in the newborn.

8. Close cooperation between the pediatrician and the surgeon is essential.

9. Many of the hundreds of patients in whom the condition was first observed at autopsy would have had a fair chance of surviving if the abnormality had been diagnosed early and given proper surgical treatment.

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DYSENTERIC BACTEREMIA

WITH A REPORT OF THREE CASES

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In the classic description of bacillary dysentery found in the textbooks on bacteriology and pathology, the statement is usually made that bacteremia due to Bacillus dysenteriae does not occur. As late as 1936, Topley and Wilson [1] made this statement concerning B. dysenteriae: "This organism, unlike Bacillus typhosus, does not invade the blood stream and cannot therefore be cultured from the blood." However, Rothman [2] reviewed the literature on this subject in 1936 and discovered that antemortem bacteremia due to B. dysenteriae has been found and reported in 16 cases. He added an additional case of his own. The organism has also been cultured at autopsy from the blood, the liver and the spleen and in several instances from the mesenteric lymph nodes.

Many investigators have undertaken to secure routine blood cultures in cases of bacillary dysentery. Duval [3] reported 43 cases of Shiga dysentery with negative blood cultures, but in 1 case he secured a culture of the bacillus from the liver and the mesenteric lymph nodes at autopsy. Dudgeon [4] made blood cultures in 145 cases of acute dysentery in Macedonia during the World War but failed to recover the organism, while Fränkel [5] made 49 blood cultures and in only 1 case was able to obtain a pure culture of the Hiss-Russell Y dysentery bacillus. Although cases of dysenteric bacteremia are undoubtedly overlooked

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2. Rothman, P.: J. Pediat. **9**:167, 1936.

3. Duval, C. W.: Am. Med. **4**:417, 1902.

4. Dudgeon, L. S.: B. Dysenteriae (Shiga), in A System of Bacteriology in Relation to Medicine, Privy Council, Medical Research Council, London, His Majesty's Stationery Office, 1929, vol. 4, p. 201.

5. Fränkel, E.: Deutsche med. Wchnschr. **41**:1182, 1915.

because of the failure to make routine blood cultures, the literature stresses the rarity of positive cultures in this disease.

Since January 1935, 226 patients with bacillary dysentery have been admitted to the Vanderbilt Hospital. Although blood cultures are not routinely made at this institution, 3 cases of bacteremia due to B. dysenteriae are on record among this group. In 1 of these the disease was recognized before death, while in the other 2 it was discovered at autopsy. It is because this condition is infrequently encountered that the following cases are reported.

REPORT OF CASES

CASE 1.—A 7 month old girl, whose illness had begun two days previously, was admitted to the hospital with complaint of vomiting, fever and diarrhea. The diarrhea was mild, and the stools, which numbered from four to five daily, did not contain blood. The temperature on admission was 101.2 F. Results of the general physical examination, aside from evidences of dehydration and abdominal distention, were normal. The white blood count was 12,500, and the carbon dioxide content of the blood was 56.5 volumes per cent.

The child was placed on a skimmed milk formula; fluids were supplied by clysis, and other supportive measures were used. With this regimen the vomiting ceased, the diarrhea subsided and the child appeared improved; but on the sixth day the vomiting reappeared, the temperature rose to 103 F., and she began to have from fourteen to sixteen liquid stools daily. B. dysenteriae was not isolated from the stool culture, but a blood culture was reported as showing the Hiss-Russell Y. bacillus. The patient became progressively worse and died on the tenth day of hospitalization.

At autopsy, the heart and lungs were normal except for pulmonary atelectasis. The liver showed changes compatible with fatty infiltration, and the spleen was the site of an acute tumor without necrosis. The kidneys showed only a mild parenchymatous degeneration. Beginning in the lower part of the ileum and extending distally, there was edema of the intestinal wall, with small, scattered areas of hemorrhage. The mucosa of the colon was covered with a thick, necrotic exudate, which when stripped away left a raw base. The regional lymph nodes were enlarged and edematous. Microscopically, the sections of the ileum showed extensive acute superficial necrosis of the mucosa and diffuse cellular infiltration of the mucosa and submucosa. Several thrombosed vessels were found, and the solitary follicles were hyperplastic. The germinal centers were large and had focal areas of necrosis and of leukocytic infiltration. The process in the colon was similar, though much more extensive, and very little mucosa remained. Only a thick mantle of necrotic cellular débris, fibrin and leukocytes was present. Regeneration of the mucosa was evident over some areas.

Postmortem cultures of the blood or the stools were not made in this case. The final diagnosis was : (1) acute bacillary dysentery, due to the Hiss-Russell Y bacillus, and (2) bacteremia, also due to the Hiss-Russell Y bacillus.

CASE 2.—A 2 month old girl, whose illness began acutely with profuse watery diarrhea and fever, was admitted to the hospital four days after the onset of the diarrhea. On admission the child was stuporous and showed evidence of recent loss of weight and of malnutrition. The child weighed 5 pounds and 8 ounces (2,495 Gm.), and the temperature was 104 F.; in other respects the

general physical examination showed nothing remarkable. The white blood cell count was 25,700, and there was a mild secondary anemia.

The child was given fluids intravenously and by clysis, and all food was withheld for a short time. Later, she was given a formula. During the first four days in the hospital she received five small transfusions. In spite of the measures taken, the stools numbered ten to twelve a day, and shortly after her admission they were noted to contain blood and pus. A culture of the stools made on the second day showed the Hiss-Russell Y bacillus. The fever and the diarrhea persisted unchecked, and on the eighth day in the hospital, rigidity of the neck, associated with cyanosis and deep stupor, was noted. On lumbar puncture the sugar content of the spinal fluid was found to be 25 mg. per hundred cubic centimeters, while the remaining data on the spinal fluid were within normal. A blood sugar determination made immediately after this showed the content to be 40 mg. per hundred cubic centimeters. Although dextrose was supplied and other supportive measures were taken, the child died that day.

At autopsy, the heart was normal, and the lungs showed only a few small subpleural hemorrhages, together with some small noninfected thrombi in the pulmonary arterioles. There were venous congestion of all the abdominal viscera and acute mesenteric adenitis. The liver, spleen and kidneys presented the picture of venous congestion, with edema of the latter organ. The ileum showed congestion and edema of the submucosa and mucosa. Beginning at the cecum and extending distally, a widespread and confluent ulceration of the mucosa, with areas of hemorrhage and deep congestion, was found. There was no evidence of a pseudomembrane, and the ulcerations did not extend into the submucosa. The lesions became more extensive and larger as one moved distally, so that in the sigmoid flexure of the colon areas of ulceration as wide as 2 or 3 cm. could be seen. From the midportion of the transverse colon on, practically no mucosa remained, but only the slick, ulcerated and hemorrhagic submucosa was visible. The microscopic picture of the colon was that of widespread, confluently ulcerative and necrotizing colitis, with a sloughing-off of the necrotic mucosa and a marked leukocytic infiltration of the submucosa and muscularis. The muscularis and serosa were intact but marked by edema and congestion, and over the serosa there were little clumps of fibrinous exudate without evidence of infection. The liver showed small focal areas of necrosis, and the spleen, the typical microscopic picture of an acute splenic tumor.

A postmortem blood culture resulted in the isolation of a gram-negative, nonmotile bacillus which agglutinated a fresh stock antiserum of the Hiss-Russell Y bacillus in dilutions of 1:640 and a stock antiserum of Bacillus of Flexner in dilutions of 1:640. A culture of the mucosa of the colon produced a similar organism, which gave agglutinations of 1:320 and 1:160.

The final diagnosis was: (1) acute ulcerative colitis, due to the Hiss-Russell Y bacillus and to B. dysenteriae Flexner; (2) bacteremia, also due to the Y bacillus and to B. dysenteriae Flexner; (3) acute mesenteric adenitis; (4) hemorrhages in the lungs and spleen, and (5) focal necrosis of the liver.

CASE 3.—A 6 month old girl entered the hospital on the sixth day of illness characterized by anorexia, fever and diarrhea. The diarrhea had not been marked prior to admission, but very shortly after entering the hospital the infant began to have blood-tinged stools every twenty or thirty minutes. The temperature on admission was 100.8 F., and the general physical examination revealed a distended and apparently tender abdomen and a palpable liver as the only pathologic conditions. There was no anemia, but the white blood cell count

was 28,000, with 68 per cent neutrophils. Throughout the first day the child continued to pass frequent liquid stools, which were accompanied by tenesmus and pain. Late in the evening she had a generalized convulsion, and her temperature was 107 F. In spite of efforts to reduce the temperature, it remained around 105 F. throughout the night, and the child was stuporous and cyanotic. Death occurred early the next morning, less than twenty-four hours after admission. Cultures of the stools, reported on after the patient's death, yielded the Hiss-Russell Y bacillus.

At autopsy, the lungs were edematous and deeply congested, and there were a few small subpleural and subepicardial hemorrhages. The liver and spleen showed evidence of acute passive congestion, and there was acute mesenteric adenitis. Beginning in the proximal ileum, a number of large, actively phagocytic mononuclear cells were seen in the mucosa and in the submucosa, together with a number of polymorphonuclear cells, plasma cells and lymphocytes. There were engorgement of the capillaries and marked hyperplasia of the lymph follicles, as well as edema of the submucosa. The same cellular infiltration was apparent in the colon, and, in addition, many areas of ulceration were seen microscopically, though these were not apparent grossly. Along the roof of the submucosa, there were a few small and shallow ulcers with necrosis at their bases, and many of the solitary follicles showed superficial ulceration. Many areas of hemorrhage were apparent in the submucosa. The muscularis was edematous and congested but was intact.

A blood culture, made at the time of the autopsy (one hour after death), gave a gram-negative, nonmotile bacillus which produced acid on dextrose and mannitol and which agglutinated a stock antiserum of the Hiss-Russell Y bacillus in dilutions of 1:500. A similar organism was cultured from the mucous membrane of the colon, and this gave agglutination in dilutions of 1:1,000.

The final diagnosis was: (1) acute ulcerative ileocolitis due to the Hiss-Russell Y bacillus. (2) bacteremia, due to the Hiss-Russell Y bacillus, and (3) acute mesenteric adenitis.

SUMMARY

Although routine blood cultures in cases of bacillary dysentery have been somewhat disappointing in their results, a positive culture is of material aid in establishing a diagnosis in cases which present unusual features. This point is of particular interest in communities where numerous cases of bacillary dysentery are encountered each year. The similarity between bacillary dysentery and some forms of typhoid fever makes the added means of diagnosis valuable.

HEMORRHAGIC PURPURA IN SCARLET FEVER

A REPORT OF TWO CASES

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Hemorrhagic conditions in scarlet fever fortunately are rare. References to them in current textbooks are brief or absent and are often coupled with the statement that some of the cases reported may have been instances of hemorrhagic smallpox. In a survey of the literature of the past thirty years, about 62 cases of hemorrhagic purpura and fulminating purpura which occurred during or after scarlet fever have been found. Most of the references have been to case reports. In a study of the cases of 5,000 patients with scarlet fever admitted to the Durand Hospital during a period of twenty years, only 2 such cases were observed. The purpose of this paper is to report these 2 cases and to discuss in a brief manner some of the pertinent questions relating to the condition.

Fulminating purpura as a complication of scarlet fever is a type of disease usually rapidly fatal and characterized by a sudden onset with chilliness, high fever, great prostration and vomiting. Ecchymoses of large size, often symmetrically placed, appear with remarkable rapidity, and within a few hours an entire extremity or the greater part of the trunk may assume a red-black color. The skin is hard and edematous and may exhibit bullae containing a bloody serous fluid. Gangrene may develop. Death takes place as a rule after from twelve to twenty-four hours, sometimes after three or four days, with cerebral symptoms ending in coma. Most of the patients with the typical syndrome have been children; in many of them the condition developed during convalescence from scarlet fever. Guelliot,[1] in 1884, was the first to describe the condition; it was more carefully studied by Henoch.[2] There was no hemorrhage from the mucous membranes in Henoch's cases, but since the appearance of his paper, in 1886, a number of cases in which there was hemorrhage from various mucous membranes have been reported.

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1. Guelliot, A.: Note sur trois cas de purpura infectieux foudroyant, Union méd. et scient. du nord-est **8**:25, 1884.

2. Henoch: Ueber Purpura fulminans, Prag. med. Wchnschr. **11**:494, 1886.

Hemorrhagic purpura comes on usually after the subsidence of the acute symptoms of scarlet fever, and not infrequently during convalescence. In most cases it develops during the second or third week, most commonly from the fourteenth to the twentieth day. A few cases have been reported in which it occurred earlier, and occasionally it has been reported as developing later than the fourth week. There are no distinct premonitory signs by which the supervention of purpura can be foretold. The attack of scarlet fever usually is mild or moderately severe. In some cases cervical adenitis, tonsillitis or rhinitis, accompanied by a slight febrile disturbance with albuminuria, may precede the cutaneous hemorrhages or the onset of bleeding from the mucous membranes. In most instances, the earliest indication of the hemorrhagic condition is the appearance of bruiselike ecchymoses on the lower limbs in the region of the sacrum, on the buttocks, over the trochanters or the iliac crests and at the points of greatest pressure. Often they occur on the cheeks, nose, ears, abdomen and shoulders. Associated with the larger bruises, a generalized purpuric eruption may appear on the body and on the visible mucous membranes. The lesions range in size from minute petechiae to large confluent blotches, which are bright colored at first but which later become a dusky purple. Hemorrhages from mucous membranes may or may not accompany the extravasations into the skin. The most frequent type is epistaxis; hematuria and hemorrhages from the gums, the stomach and the bowels may also occur. There seems to be a relation between scarlatinal purpura and gangrene, which occasionally supervenes during the course of scarlet fever. Local necroses of the toes, fingers, nose and cheeks and in some cases gangrene of one or both lower extremities have been reported. Dick, Miller and Edmondson [3] in 1934 reviewed the literature and found 15 cases of gangrene associated with scarlet fever; they also reported a case of their own.

From a consideration of the two forms of purpura which occur during or after scarlet fever, it would seem that the difference is one of degree only. Purpuric forms are known in all specific fevers, especially in typhus, smallpox and epidemic meningitis, and less often in typhoid fever, measles, diphtheria, pneumonia and septicemia. Crocker [4] believes that in the production of all the severe forms of purpura and in that of many of the milder forms there is much evidence of the importance of a

3. Dick, G. F.; Miller, E. M., and Edmondson, H.: Severe Purpura with Gangrene of the Lower Extremity Following Scarlet Fever, Am. J. Dis. Child. **47:** 374 (Feb.) 1934.

4. Crocker, H. R.: Diseases of the Skin, Philadelphia, P. Blakiston's Son & Co., 1903.

toxin, whether of bacterial or of other origin. On the basis of an experimental study of the problem in animals, Pulvertaft [5] expressed the belief that streptococcus toxin is the main factor and that whenever purpura is associated with acute streptococcic infection, either directly or indirectly, it is due to the toxin of the streptococcus. However, it is known that in scarlet fever the toxin is formed in greatest quantity early in the disease; and since the purpura usually occurs during convalescence, it would seem that its occurrence might be explained on the basis of damage to the endothelium of the blood vessels. That the toxin of scarlet fever is capable of inflicting damage on the capillaries is demonstrated by both clinical and experimental evidence. The production of small petechial hemorrhages at the bend of the elbow, where congestion of the arm is induced by a constricting band, is generally accepted as a sign of diminished capillary resistance. The small hemorrhagic streaks often present in the flexures of the joints after the scarlatinal rash has faded afford evidence of the same kind. It is also known from studies with a capillary microscope that up to forty days after the disappearance of the eruption of scarlet fever the capillaries do not function properly. This evidence suggests that there is a vascular element in the production of the purpura.

Jones and Tocantins [6] stated: "Capillary hyperpermeability, or capillary weakness, is essential for the production of hemorrhagic phenomena, which may occur if this condition is present alone or if both capillary hyperpermeability and platelet deficiency are found."

Adami [7] expressed the opinion that the primary change is in the endothelium of the vessels, with degenerative changes in their walls. Some clinicians have thought that hemorrhages occur too rapidly to be the result of degenerative changes, but it has been found that the endothelium of the blood vessels may show alteration within a few minutes after the introduction of toxin. If, as it seems, the hemorrhagic condition is due to the action of scarlatinal toxin on the endothelium of the blood vessels, it would be interesting to note whether it occurs in scarlet fever which is treated early and with adequate doses of scarlet fever antitoxin.

The histologic changes in the kidneys in early scarlatinal nephritis also afford strong confirmatory evidence of vascular change. The earliest change is in the endothelium of the vessels which constitute the

5. Pulvertaft, R. J. V.: An Examination of the Pathological Effects of Streptococcal Toxin and Hemolysin on Rabbits with Especial Reference to the Etiology of Purpura Fulminans, Lancet **2**:318, 1929.

6. Jones, H. W., and Tocantins, L.: The Treatment of Purpura Hemorrhagica, J. A. M. A. **100**:83 (Jan. 14) 1933.

7. Adami, J. G.: Principles of Pathology, ed. 2, Philadelphia, Lea & Febiger, 1910, vol. 2, p. 912.

glomerular tufts. The endothelial swelling tends to obstruct and even to block the linings of the capillaries. An exudation into Bowman's capsule may force the tufts down toward the hilus; blood may be extravasated, and in some cases true hemorrhage may occur. It is also a striking fact that both nephritis and purpura are most likely to occur in the second or third week of scarlet fever. This may be more than a coincidence and has led to the suggestion that scarlatinal nephritis may be a purpuric manifestation. In fact, Frank [8] defined scarlatinal nephritis as renal purpura. However, in postscarlatinal purpura clinical evidence of renal involvement is often, but not always, present.

The consensus of the various workers seems to be that in the production of the hemorrhagic condition in scarlet fever or in other specific fevers the hemorrhagic diathesis is not of much importance and cannot be attributed to the activation of a preexisting but latent hemorrhagic tendency. Henoch [9] said that an attack of purpura shortly before scarlet fever does not give rise to any special tendency to hemorrhagic complications, and he cited a case of his own in support of this statement. Box [10] also stated that a patient of his with a hemorrhagic diathesis passed through an attack of scarlet fever without any complication.

The studies of the blood in the cases reported in the literature have shown a considerable leukocytosis, which usually diminishes if the condition approaches a fatal termination. The leukocytosis is of the polymorphonuclear type, and such cells may form 80 per cent or more of the total. The leukocyte count generally varies from 18,000 to 80,000. The proper leukocytosis of scarlet fever occurs at the onset of the disease, and at the usual time for the onset of purpura the blood count should be normal or nearly so. In most of the cases in which platelet counts have been recorded, there has been a sharp reduction. The bleeding time when recorded has usually been prolonged.

Autopsies fail to reveal anything that would suggest a possible cause for the hemorrhages. In some instances no internal hemorrhages have been found, but frequently petechial or even larger extravasations have been noted in the serous and mucous membranes, including that of the bladder, and in some cases blood-stained pleural or peritoneal exudate has been found. Hemorrhages have also been found in the mediastinum, in the broad ligaments and in the ovaries.

REPORT OF CASES

CASE 1.—A boy 4 years of age, previously of good health, was suddenly taken sick on Feb. 25, 1922, with fever, vomiting and sore throat. The next day he

8. Frank, E., in Schittenhelm, A.: Handbuch der Krankheiten des Blutes und der blutbildenden Organe, Berlin, Julius Springer, 1925, vol. 2, p. 464.

9. Henoch, E.: Lectures on Children's Diseases, translated from ed. 4 by J. Thomson, New Sydenham Society, London, 1889.

10. Box, C. R.: On Complications of the Specific Fevers, Lancet **1**:1217, 1933.

had a general scarlatinal eruption. On admission, February 28, he had a temperature of 102.6 F. and a pulse rate of 120. The white blood leukocyte count was 24,000, with 88 per cent of the cells polymorphonuclear. The urine was normal. The throat was red, with small patches of exudate on both tonsils. The rash was fading.

The boy continued to have a moderate fever (temperature 99.8 to 100.6 F.), accompanied by slight enlargement of the cervical lymph glands, limited mucopurulent nasal discharge and in one ear transient pain which disappeared without perforation of the tympanum. On March 23, twenty-six days after the onset of scarlet fever, blood appeared in the stool, bright red blood oozed from the nostrils and petechial hemorrhages were seen scattered over the skin, most abundantly over the shoulders and back. The temperature was 100 F. and the pulse rate 110. During the next three days, March 23 to 25, large amounts of blood with dark clots were passed from the bowels, blood was discharged from the nose and mouth and more of the petechial hemorrhages appeared on the arms, the chest and the abdomen. The temperature varied from 99.6 to 102.4 F., and the pulse rate from 130 to 140. There was no blood in the urine. The leukocyte count was 18,500 and the percentage of hemoglobin fell to 50. No platelet count was recorded. From March 25 to 28 the bleeding gradually became less, and after March 29 no bleeding occurred. The petechial hemorrhages gradually faded, and the general condition improved. Between March 23 and March 27, 15 cc. of fresh human serum and 120 cc. of whole blood from the boy's father were injected intramuscularly in five doses. Calcium lactate in doses of 20 grains (1.29 Gm.) was given by mouth four times a day from March 23 to April 11. By April 3 the leukocyte count had fallen to 5,300, the red cells numbered 1,980,000 and the amount of hemoglobin was 55 per cent. Improvement was uninterrupted, and the boy was discharged in good condition on April 23.

CASE 2.—A girl 3½ years old, previously of good health, was taken sick with vomiting, fever and sore throat on Jan. 20, 1925. Two days later a general cutaneous eruption appeared. On admission, January 22, she was delirious; she had a typical general scarlet fever eruption, her throat was red, and her tonsils were swollen and presented patches of exudate. There was moderate cervical adenopathy. The temperature was 104.6 F. and the pulse rate 136. The number of white blood cells was 12,500, 86 per cent of which were polymorphonuclear. The urine showed a trace of albumin but was otherwise normal.

The next day the fever remained high, small hemorrhagic areas appeared in patches over the abdomen and the back, blood oozed from the nose, bloody fluid was vomited and blood appeared in the stool. The red cell count was 2,900,000, and the hemoglobin content was 50 per cent. There was blood in the urine. The pulse became more rapid and feeble, and death occurred within three days after the onset. Cultures of the blood obtained from puncture of the heart soon after death yielded abundant hemolytic streptococci. Autopsy was not permitted.

SUMMARY

Two cases of hemorrhagic purpura complicating scarlet fever, which were observed in a study of 5,000 cases, are reported. In 1 case the complicating purpura developed on the twenty-sixth day of the disease and the patient recovered; in the other it occurred on the fourth day of the disease, was of the fulminating type and resulted in death three days after the onset.

LEUKEMIA OF UNDETERMINED TYPE SUGGESTING MIXED LEUKEMIA

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Leukemia of all types is characterized by hyperplasia of the tissues which produce the white cells, usually accompanied by the escape of immature forms of cell into the circulating blood. Various types of leukemia have been identified, according to the special type of tissue which is predominantly involved and the type of immature cell in the circulating blood. Thus, there are the so-called myelocytic form, the lymphocytic form and the monocytic form. Other forms have been described, which are not so well established, for example, eosinophilic and basophilic leukemia. With chronic leukemia the recognition of the type is usually easy, but with the acute form the predominant cells are apt to be very immature—and the more immature they are the more difficult the identification of the type becomes. The extremely immature cells resemble each other closely and lack the characteristics of the mature cell by which the type can be readily identified.

Even with acute leukemia, however, it is usually possible to make the diagnosis from study of the circulating blood, and it is even easier to do so from examination of tissue. However, there is some doubt as to whether the criteria employed by some in this differential diagnosis are as trustworthy as is claimed. The following case, in which the diagnosis remained uncertain even after autopsy, is reported to illustrate the difficulties which may be encountered.

REPORT OF A CASE

E. L. A., a Negro girl aged 3 years, came under the care of one of us (J. A. W.) on March 18, 1936, because of fever and lumps about the neck. There was a history of diarrhea in the first year of her life, colds each winter and measles in the second year. Several weeks before admission she suffered a burn on the dorsum of the left foot, which became infected. Subsequently the glands in the

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Drs. O. H. Perry Pepper and Thomas Fitz-Hugh, of the University of Pennsylvania Hospital, and Dr. R. P. Custer, of the Philadelphia General Hospital, assisted in studying the slides and in preparing the manuscript.

neck became swollen, then those in the axillas and finally those in the groins. About three weeks later the abdomen became enlarged. More recently there had been some coughing. On examination, the child was well developed and apparently not acutely ill; she was slightly dyspneic. The face was edematous, the tonsils were large and ragged, and the mucous membranes were pale, with no hemorrhage. The cervical lymph nodes were swollen beyond the normal contour of the neck. The maxillary, axillary and inguinal glands seemed enlarged on inspection and on palpation. Cardiac dulness was noted 1 cm. outside the left nipple line. A systolic murmur at the fourth rib was referred to the back. No definite abnormality was observed in the lungs. The liver extended 4 finger-breadths below the costal margin. The spleen extended into the pelvis. The eye-grounds showed old and new hemorrhagic areas. The red cell count was 2,220,000 per cubic millimeter and the hemoglobin content (Sahli) 28 per cent; the white cell count was 384,000 per cubic millimeters, with 16 per cent polymorphonuclears, 47 per cent lymphocytes, 3 per cent myelocytes, 27 per cent promyelocytes and 7 per cent myeloblasts. An occasional eosinophilic and basophilic myelocyte was

Fig. 1.—E. A., a Negro girl aged 3 years.

found. Achromia of grade 3 was present. The platelets numbered 10,000 per cubic millimeter. With a peroxidase stain the granulocytes were estimated at 52 per cent and the lymphocytes (nongranular) at 48 per cent. The urine contained no blood and only a faint trace of albumin. The rectal temperature was 100 F.

The temperature was elevated in the evenings to 101 and occasionally to 103 F. The patient took her feedings well until just before death, which occurred on April 14. At no time was there any bleeding from the nose, mouth, bowels or kidneys, nor were there any purpuric spots.

Blood counts made on eighteen different days showed an almost steady decline in the number of red cells, the count being 2,200,000 on admission and 740,000 on the day of death. The white cell count increased from 394,000 to 651,000. Eighteen oxidase preparations showed slight variations in the differential count throughout the course of the disease.

Because of the conflicting elements in the picture, a diagnosis could not be made. Ordway, Gorham and Beebe [1] advised the application of the adage "A man is known by the company he keeps." Judging from the preponderance of

1. Ordway, T.; Gorham, L. W., and Beebe, R. T.: Leukemia, in Christian, H. A., and Mackenzie, J.: Oxford Medicine, New York, Oxford University Press, 1928, vol. 2, p. 752.

mature lymphocytes over mature neutrophils, this disease should be a lymphatic leukemia. But with 50 per cent of the white cells showing oxidase granules, the possibility of myelogenous leukemia cannot be ignored. After studying the stained spreads, Pepper [2] wrote us that he had never seen blood which so strongly suggested a mixed leukemia, with both myelocytic and lymphocytic series involved. Fitz-Hugh [3] suggested that monocytic leukemia would explain the presence of oxidase-positive cells. He stated in support of this that ". . . the oxidase-positive cells show a marked tendency of the granules to clump in small half moons and masses opposite the *Hof* of the nucleus." Kracke and Garver [4] also claimed that there is evidence that in monocytic leukemia the monocyte has its origin in the bone marrow. Bray [5] considered this a case of myelogenous leukemia

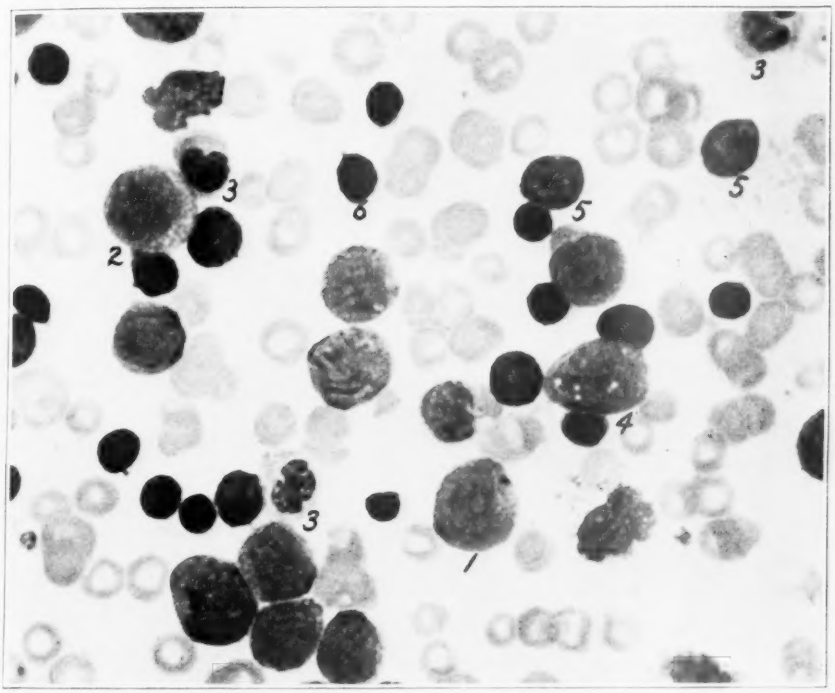

Fig. 2.—A typical field in a smear of peripheral blood, showing the following cells: *1,* myeloblasts; *2,* a promyelocyte; *3,* metamyelocytes; *4,* an immature monocyte; *5,* a lymphoblast, and *6,* lymphocytes. No myelocytes or nucleated red blood cells appear in this field, but they are present elsewhere. Wright's stain; × 698.

and explained the presence of an excessive number of lymphocytes as due to ". . . the disturbance of the lymphoid tissue caused by the infiltration of the myelocytic cells and the formation of leukopoietic nodules or centers in that tissue and elsewhere."

2. Pepper, O. H. P.: Personal communication to the authors.

3. Fitz-Hugh, T., Jr.: Personal communication to O. H. P. Pepper.

4. Kracke, R. R., and Garver, H.: The Differential Diagnosis of the Leukemic States, J. A. M. A. **104**:697 (March 2) 1935.

5. Bray, W. E.: Personal communication to the authors.

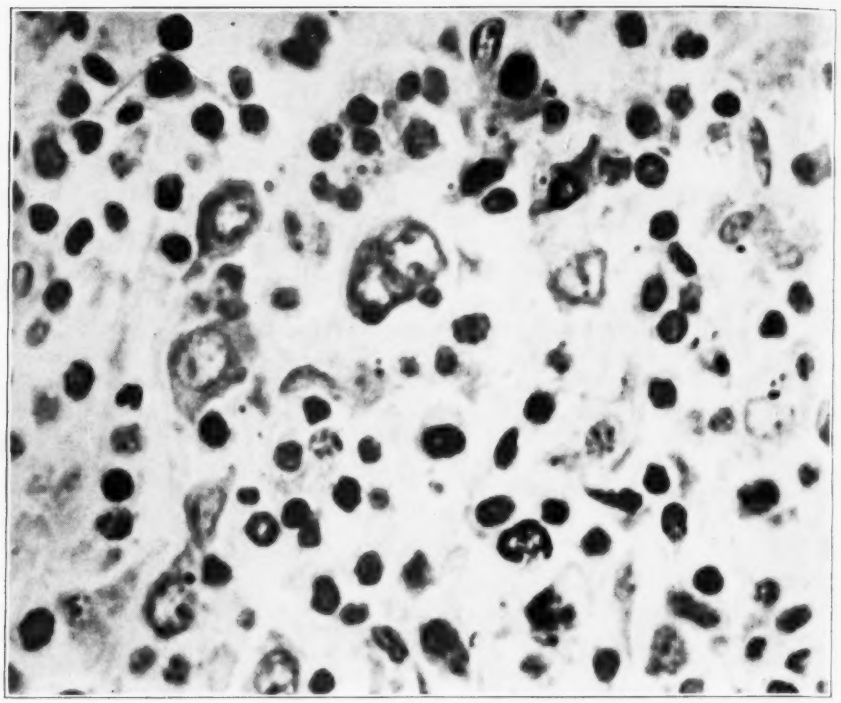

Fig. 3.—A section of spleen showing the various types of cells throughout the sinuses and pulp, the former being so full of cells that their contours are ill defined. Here the hyperplasia of sinal endothelium with budding and liberation of large undifferentiated cells is conspicuous. Giemsa's stain; × 920.

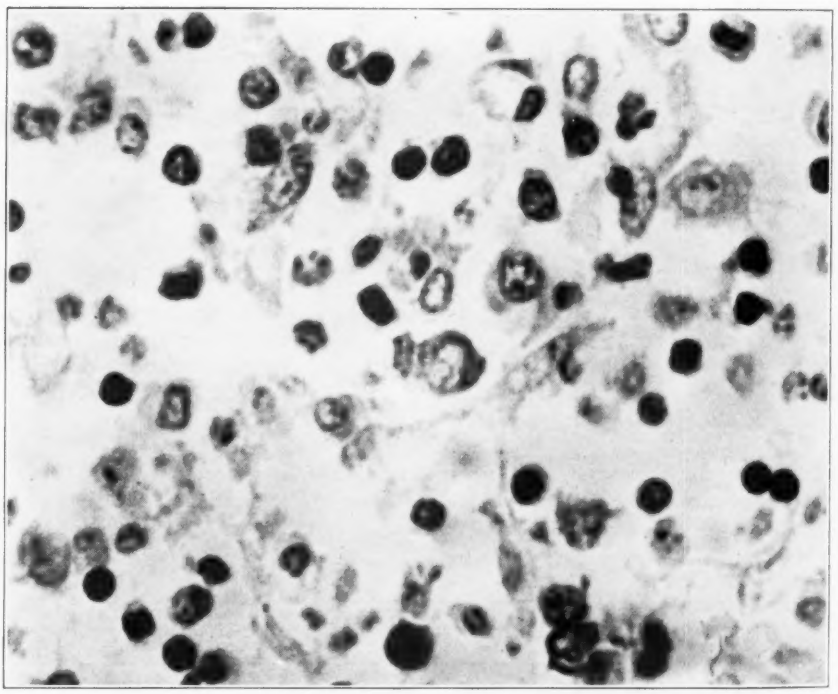

Fig. 4.—Loose area in the medullary cord of a lymph node, showing a background of reticulum cells and interspersion of granulocytes, monocytes, lymphocytes and normoblasts. Giemsa's stain; × 920.

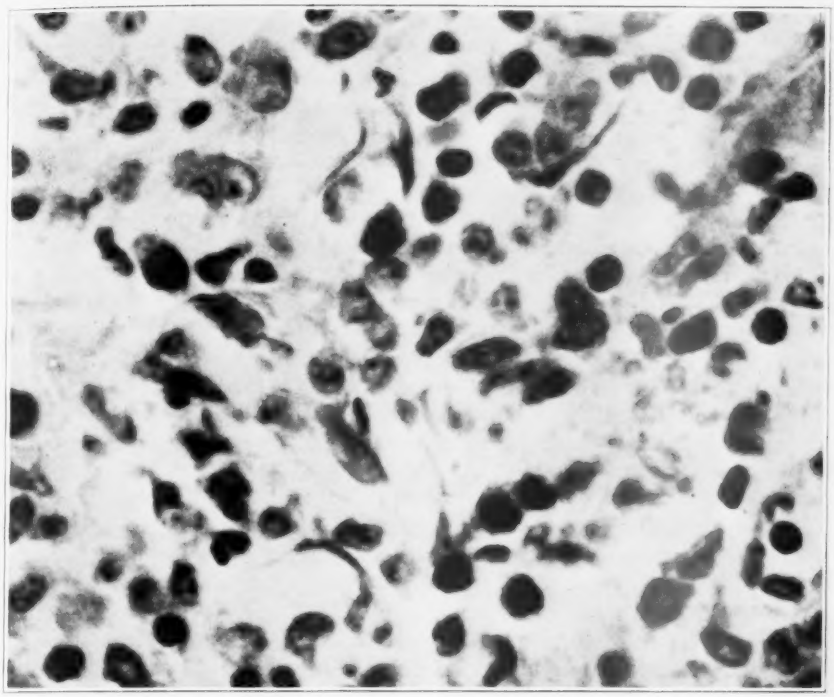

Fig. 5.—Section of the liver from an area of particularly active metaplasia, illustrating proliferation of cells of the reticuloendothelial system and differentiation toward the various types of cells noted in the peripheral blood. Giemsa's stain; × 920.

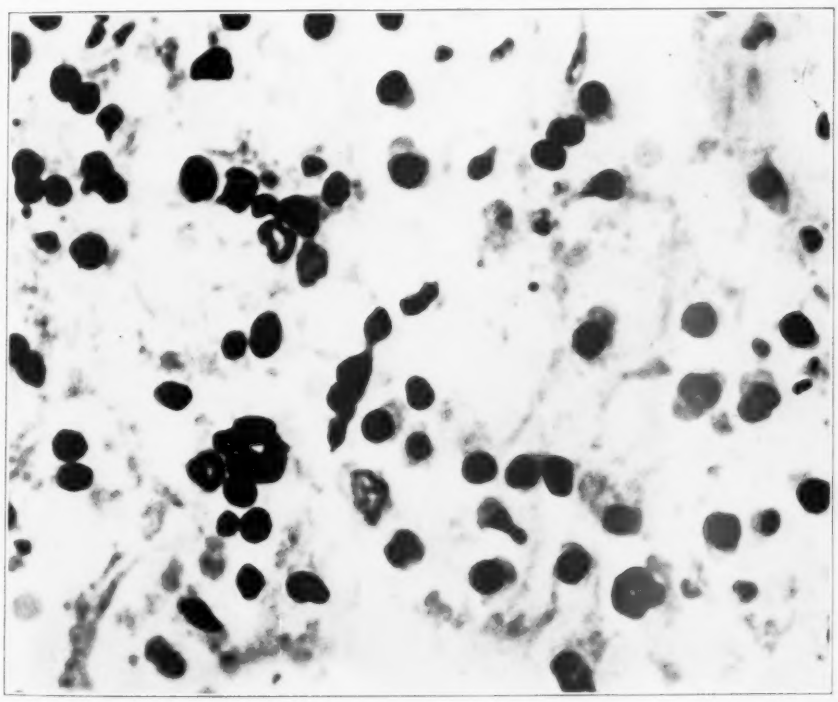

Fig. 6.—Bone marrow showing loosely scattered late erythroblasts, normoblasts and lymphocytes, with granular débris in the interstices. Several degenerated megakaryocytes are present in the field. Giesma's stain; × 920.

Blood smears, as well as specimens obtained at a limited autopsy, were reported on by Custer [6] as follows:

"*Blood.*—The bulk of undifferentiated forms I believe to be myeloblasts; I can demonstrate adequate transition through promyelocytes, myelocytes and metamyelocytes. A practically equal number of fairly well differentiated lymphocytes are present, as well as an occasional lymphoblast. A few monocytes, normal and young, are encountered; late erythroblasts and normoblasts are sparsely distributed.

"*Spleen and Lymph Node.*—These present practically identical histologic pictures. The normal pattern of each is entirely lost. There is a background of actively proliferating cells of the reticuloendothelial system; the other elements compose a heterogeneous admixture of lymphocytes, immature granulocytes, cells of the monocyte-macrophage variety and occasional erythroblasts, as well as a scattering of free undifferentiated forms.

"*Liver.*—Massive leukemic metaplasia is encountered, most marked in the neighborhood of the portal triads and occurring to a lesser degree within the sinusoids of the lobules. The cellular components are similar to those of the spleen and lymph node.

"*Bone Marrow (Ribs).*—Practically no fat is present; the cells are largely late erythroblasts and normoblasts, which are loosely arranged in a background of reticular fibrillae and finely granular cellular debris. A few immature granulocytes remain, and there is a minor degree of lymphoid infiltration. Degenerated megakaryocytes are occasionally encountered. The picture suggests degeneration or exhaustion of a previously tightly packed marrow, the more robust erythrogenic forms being the chief survivors."

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6. Custer, R. P.: Personal communication to the authors.

Progress in Pediatrics

ADRENAL NEUROBLASTOMA

REPORT OF A CASE AND REVIEW OF THE LITERATURE

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Adrenal neuroblastomas occur almost entirely in infants and in children. They constitute an entity the clinical manifestations of which are usually pronounced. Since the number of reported cases in the literature is about 275, the tumors are still to be classed as a medical rarity. Under these conditions it is likely that in many of the cases the diagnosis is first made late in the illness, when metastases are pronounced, or post mortem. Although it must be admitted that treatment up to this time has proved almost entirely ineffective, early recognition should still be a desideratum. Consequently, we feel warranted in reporting an additional case of adrenal neuroblastoma, with a review of the literature.

Virchow [1] is generally credited as being the first to recognize the nature of these adrenal tumors in children. Before his work they were not considered to be of nervous origin but were thought to be round cell sarcomas of the adrenal gland. Virchow referred to them as gliomas. It is noteworthy that even after this pronouncement they were still frequently mentioned as sarcomas. In 1885 Dalton [2] published the first report of a case in which the tumor was so completely described histologically that little doubt remained that it was a neuroblastoma. In

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From the Department of Pediatrics of Hahnemann Medical College and St. Luke's and Children's Hospitals.

1. Virchow, R.: Die krankhaften Geschwülste, Berlin, A. Hirschwald, 1863-1867, vol. 2, p. 150.

2. Dalton, N.: Infiltrating Growth in Liver and Suprarenal Capsule, Tr. Path. Soc. London **36**:247, 1885.

1891 Marchand [3] reported the second case in which the diagnosis was unmistakable. This was the first instance in which a tumor of this type was recognized as a nerve tissue neoplasm. Before 1910 a small number of the tumors were reported under various designations, and considerable controversy existed over their nature and their embryonic origin. In 1910 Wright [4] in an epochal paper established rather definitely the theory of the neuroblastic origin of these tumors. In fact, he was the first worker to use the term neuroblastoma. Pepper [5] in 1901 and Hutchinson [6] in 1907 described effectively the clinical picture of the disease. After publication of these descriptions, the so-called Pepper and Hutchinson types were recognized on the basis of the observations presented. Frew [7] in 1910 reported a series of 51 cases of neuroblastoma, including several from the literature. These were reported under the title "Cancer of the Adrenal Glands." Wahl [8] in 1914, Dunn [9] in 1915 and Lehman [10] in 1917 produced exhaustive reviews of the literature, each bringing his summary up to date. In 1933 Scott, Oliver and Oliver [11] reviewed the literature, which was once more covered up to date. They also presented an elaborate classification. Since then over 100 additional cases have been reported. These we have tabulated. While the majority of cases were reported singly, there have been a number of notable collections: Nakatani [12] collected 8 cases, Blacklock [13]

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3. Marchand, F., in Internationale Beiträge zur wissenschaftlichen Medizin: Festschrift, Rudolf Virchow gewidmet zur Vollendung seines 70 Lebensjahres, Berlin, 1891, vol. 1, p. 578.

4. Wright, J. H.: Neurocytoma or Neuroblastoma, J. Exper. Med. **12**:556, 1910.

5. Pepper, W. A.: A Study of Congenital Sarcoma of the Liver and Suprarenal, Am. J. M. Sc. **121**:287, 1901.

6. Hutchinson, R.: Suprarenal Sarcoma in Children with Metastases to Skull, Quart. J. Med. **1**:33, 1907.

7. Frew, R. S.: On Carcinoma Origination in the Suprarenal Medulla in Children, Quart. J. Med. **4**:123, 1911.

8. Wahl, H. R.: Neuroblastoma with a Study of a Case Illustrating the Three Types, J. M. Research **30**:205, 1914.

9. Dunn, J. S.: Neuroblastoma and Ganglioneuroma of the Suprarenal Body, J. Path. & Bact. **19**:456, 1915.

10. Lehman, E. P.: Neuroblastoma with Report of a Case, J. M. Research **36**: 309, 1917.

11. Scott, E.; Oliver, M. G., and Oliver, M. H.: Sympathetic Tumors of the Adrenal Medulla, with Report of Four Cases, Am. J. Cancer **17**:396, 1933.

12. Nakatani, M.: Fälle von Neuroblastoma sympathicum, Tr. Soc. path. jap. **24**:581, 1934.

13. Blacklock, J. W. S.: Neurogenic Tumors of the Sympathetic System in Children, J. Path. & Bact. **34**:27, 1934.

16 and Askin and Geschickter [14] 19. These series should be studied directly by those interested.

It must be stated that in some of the cases which have been reported in the past the diagnosis is open to question. Kato and Wachter [15] in a recent paper questioned whether a considerable number of the reported cases are instances of true neuroblastoma. There are some in which the diagnosis seemed clinically authentic but in which histologic observations were incomplete or even absent. Consequently the total number of cases reported here is essentially an approximation.

An explanation for the fact that varied types of tumor arise from the adrenal gland is found by reference to the development of that gland. The adrenal cortex is derived from the mesoderm of the wolffian ridge; the alteration of secondary sex characteristics associated with certain cortical tumors is consequently almost an expected phenomenon. The adrenal medulla has an entirely different origin, arising from the ectoderm of the primitive neural crest. The neural crest gives rise to two types of cells: the stationary cells, which develop into the dorsal root ganglion cells, and the migrating cells, from which the sympathetic ganglion cytons and the chromaffin cells of the adrenal medulla are derived. The undifferentiated migratory cells are sympathetic neuroblasts. Tumors composed of undifferentiated neural elements are consequently neuroblastomas and are highly malignant. Tumors made up of differentiated cells are benign, being formed either of mature nerve cells and fibers (ganglioneuroma) or of chromaffin cells (paraganglioma or chromaffin cell tumor [pheochromocytoma]).

Neuroblastomas may arise either in the adrenal medulla or in the immediate neighborhood. They are extremely cellular; they are composed of small round cells with nuclei that resemble lymphocytes; these cells form rosettes by their circular or columnar arrangement around a fine fibrillar network. Metastases are widespread; depending on the distribution, two clinical types of neuroblasts are recognized, the Pepper type, with mesenteric nodes and involvement predominantly in the liver, and the Hutchinson type, with involvement of the skull and particularly with periorbital metastases. Occasionally the primary tumor mass may resemble a ganglioneuroma, with metastases having a typical neuroblastomatous formation; of such a type was that which will presently be described.

A rather complicated terminology exists for the naming of these tumors. This terminology is based in part on classification designating

14. Askin, J. A., and Geschickter, C. F.: Suprarenal Neuroblastoma in Children, J. Pediat. **7**:157, 1935.

15. Kato, K., and Wachter, H. E.: Adrenal Sympathicoblastoma in Children, J. Pediat. **12**:449, 1938.

the degree of differentiation of the tumor and in part on a number of synonyms introduced by various earlier workers. Scott, Oliver and Oliver constructed a classification on the basis of the degree of differentiation.

Class I consists of completely undifferentiated tumors; class II consists of incompletely differentiated tumors, and class III embraces tumors which are completely differentiated and as such cannot be considered true neuroblastomas. This group comprises ganglioneuromas and chromaffinomas, or paragangliomas.

For general purposes, the term adrenal neuroblastoma is used to describe all the tumors which contain undifferentiated tissue. Synonyms are sympathoblastoma, sympathogonioma, ganglioma embryonale and sympathicoblastoma.

The clinical picture in a case of neuroblastoma of the adrenal is largely dependent on the metastases. In the type described by Pepper the outstanding feature is the abdominal enlargement, which is produced by the enlargement of the retroperitoneal lymph glands plus that of the liver. The Pepper type is seen as a whole in the younger children and is prone to occur if the tumor involves the right adrenal. Under these circumstances the metastases are presumed to reach the liver via the lymphatics. In the type described by Hutchinson, which is usually seen after the second year, the metastases occur particularly to the bone, especially the skull. Here the striking changes often take place about the orbits. While there is a tendency for these types to occur, there is frequently an overlapping of the two syndromes. The Hutchinson variety is associated with profound anemia, but this may also occur with the other variety. The anemia is felt to be due to the widespread metastases in the bone marrow.

The complaints on admission are usually enlargement of the abdomen, pallor, wasting and listlessness. Swelling of the head and pain in the extremities are also noted rather frequently. At times an indefinite elevation of temperature is present. In cases in which the skull is involved, proptosis and ecchymosis of the upper lid occur. Owing to the localization of the metastases in the orbital wall, pressure on the optic nerve with resulting atrophy is found. Roentgenograms of the skull and of the long bones frequently show rarefaction with an overlying periosteal reaction.

Diastasis of the sutures of the skull is usually seen when the head is involved. It has been shown by Kato and Wachter [15] that the histologic picture of the metastases in the bone is identical with that of the original tumor. The pancreas, spleen, lungs and heart have all been the site of metastases. The regional lymph nodes are frequently involved.

Differential diagnosis is facilitated by the following considerations:

With tumor of the adrenal cortex the characteristic findings are hirsutism, pubertas praecox and frequently elevation of blood pressure.

Wilms' tumor usually occurs in children over 2 years of age. It responds to radiation. The tumor is frequently palpable. A pyelogram usually aids in the diagnosis. Hematuria occurs sooner or later. Involvement of the bone is rare, but if it occurs, the pelvis is the most likely site.

With lymphosarcoma, ascites is more likely to occur than with other types. The superficial lymph nodes are often involved; biopsy can be made on them. The malignant growth responds markedly to radiation.

Ovarian tumors are rather rare in children. The large tumors are freely movable; they grow out of the pelvis. Bimanual examination is a diagnostic aid. With the variety of tumors which are twisted on the pedicle, the picture is that of an acute abdominal condition with leukocytosis.

The general picture of leukemia often resembles that of an adrenal neuroblastoma. Repeated blood studies and bone marrow punctures should ultimately confirm the diagnosis.

The patient with chloroma is usually older. The associated findings are those of leukemia. It must be borne in mind that the osseous changes of lymphatic leukemia may resemble closely those of adrenal neuroblastoma.

The children with Hand-Schüller-Christian disease are usually older. The splenic enlargement is more pronounced. Studies of the blood lipoids should be helpful. Roentgen study shows large circular defects in the skull.

Ewing's sarcoma occurs late in childhood. The roentgenograms show an onion peel splitting of the layers in the periosteal reaction.

Occasionally rheumatic fever must be eliminated. However, this should be done with ease, if the entire picture is considered.

Probably the greatest difficulties occur in differentiating adrenal neuroblastoma from lymphsarcoma, acute leukemia and chloroleukemia.

The clinical course in these cases is almost universally rapid, progressing to a fatal termination. The average duration of the symptoms and signs is about two to five months. It is noteworthy that with the Pepper type, the duration is shorter and the age of the patient is also less than with the Hutchinson type. A septic temperature, profound anemia and cachexia usually set in as the metastases become advanced. Death may occur suddenly.

Irradiation produces a slight temporary response, and surgical intervention is usually followed by death within several months.

It must be mentioned, however, that in the case reported by Lehman [16] operation was done in 1916, and the patient was still living and well in 1931, fifteen years later.

We have collected 113 cases of adrenal neuroblastoma in infants and children; to the best of our knowledge, they comprise all that have been reported in the literature since the review of Scott, Oliver and Oliver. In a few cases the histopathologic observations were incomplete or microscopic examination was not made, but the age of the patient, the metastases, and the clinical course seemed to justify inclusion in the series.

We have summarized 105 of these cases according to the sex of the patient and the location and the clinical type of the tumor (table 1). Since grouping the tumors into the Hutchinson and the Pepper type is rather arbitrary, it was difficult to assign them properly in all of these cases.

TABLE 1.—*Summary of One Hundred and Five Cases of Adrenal Neuroblastoma* *

Site of Primary Tumor	Hutchinson Type	Pepper Type	Mixed Type	Uncertain Type	Total
Right adrenal	19	15	1	8	43
Left adrenal	22	11	1	8	42
Both adrenals	9	3	..	2	14
Not stated	4	1	..	1	6
Total	54	30	2	19	105
Sex incidence					
Male	23	17	1	9	50
Female	20	7	1	7	35
Not stated	11	6	..	3	20
Total	54	30	2	19	105

* The average age in the entire group of cases was 3⅝ years; the average age in the Pepper group was 1½ years.

In the Hutchinson group we included all the tumors with which there was prominent involvement of the skull. In the Pepper group we placed those associated with hepatic involvement and no osseous metastases. In the mixed group we placed the tumors associated with the metastases in the liver and in the bone but no involvement of the skull. In the uncertain group we included tumors of doubtful type.

The 8 cases of Sear [17] in which diagnosis was made largely by roentgen findings were not included in the summary.

It will be seen that the Hutchinson type of growth predominated. Boys exceeded girls, but the figures in this respect are not too significant. The average age for the entire group of patients was 3⅝ years.

16. Lehman, E. P.: Adrenal Neuroblastoma in Infancy—Fifteen Year Survival, Ann. Surg. **95**:473, 1932.

17. Tidswell, F., and Sear, H. R.: Neuroblastoma: Experiences at the Royal Alexandria Hospital for Children, Sydney, Australian & New Zealand J. Surg. **2**:370, 1933.

In general, the Pepper type of tumor occurred in the younger patients, their age being 1½ years. These observations correspond to those previously reported.

REPORT OF CASE

R. R., a 2½ year old girl of Italian parentage, came under our observation and care in the pediatric ward of the St. Luke's and Children's Hospital. She was admitted on Sept. 21 and died on Dec. 9, 1937. The chief complaint was swelling of the eyelids and abdomen, with some abdominal tenderness; there were pallor and weakness. The symptoms were recurrent in type and had been present during the previous three months.

The family history was noncontributory. There were seven other children in the family. All were living and well with the exception of one, who had a congenital cardiac disorder.

The girl was born at full term with normal delivery. The weight was 9 pounds (4,082 Gm.). The child was breast fed. She had had tonsillitis and colds during the previous winter, with full recovery; otherwise she was in good health up to the time of the present illness.

About September 7 the girl complained of pain in the abdomen, which was swollen. There was no vomiting, and the bowel movements were normal. The face and eyes were edematous. The swelling would diminish after ten or twelve hours and would apparently be absent for a day or so. On awakening the next morning the child would again show edema of the eyelids and abdomen.

Examination was made by an intern. The child was fairly well nourished. She was crying lustily and complaining of pain throughout the abdomen. This was not localized. The abdomen was distended, showing an elevation of the navel. There was no ascites. The liver was palpable, extending 3 inches (8 cm.) below the costal border. The spleen was not palpable. The teeth were normal. The tonsils were large, but not inflamed and showed no patches. The pulse was rapid and regular. There were no cardiac murmurs, and the size of the heart was normal. The lungs and respiration were normal. The upper eyelids were puffy and edematous. The pupils were normal and reacted normally. The muscle balance was normal. The nervous reflexes were full and equal, presenting negative findings. There was no glandular enlargement. The skin was somewhat pale, and the child appeared anemic. There was no jaundice. The provisional diagnosis was nephrosis. The next day, September 22, a report on the blood showed a hemoglobin content of 68 per cent and 3,500,000 red cells and 8,000 leukocytes per cubic millimeter, with 69 per cent polymorphonuclears, 30 per cent lymphocytes and 1 per cent monocytes. The color index was 0.9. The urinary examination showed a trace of albumin, coarse granular casts, occasional hyaline casts, several epithelial cells and 1 or 2 pus cells. A transfusion was given, the patient receiving 150 cc. of blood.

We saw this child for the first time on October 1 (ten days after admission, when one of us (J. L. R.) started service in the ward. An examination at that time confirmed in a general way the results of the previous examination, made by the intern. These following special notations were made: The child was fairly well nourished but anemic, and the skin was waxy. The eyes were puffy and swollen. The abdomen was large, tense and tympanitic. No localized pain or tender spots were noted. The liver was easily palpable, extending 3 inches below the right costal border, almost to the umbilicus. The edge was smooth, and the left lobe was enlarged. Because of the tense and resistant abdomen the spleen could not be outlined. There was no edema or swelling of the lower extremities. Cervical and inguinal adenopathy was present.

TABLE 2.—*Data in Reported Cases of Adrenal Neuroblastoma*

Author	Sex	Age	Site	Metastases
Geisler, G., and Schein, H.: Arch. f. Kinderh. **91**: 54 (July 25) 1930	F	6½ mo.	Right adrenal	Liver
Meyer, A. H.: Ugesk. f. læger **93**: 135 (Feb. 5) 1931	F	3 yr.	Right adrenal	Skull, liver, retroperitoneal glands
Lautier and Sansinenea: Strasbourg méd. **90**: 747 (Nov. 25) 1930	M	4 yr.	No autopsy	Orbit, bone; preauricular, axillary and inguinal glands
Rome, M.: Rev. belge sc. méd. **3**: 853 (Aug.-Sept.) 1931	F	3½ yr.	Left adrenal	Skull
Peterman, M. G.: Am. J. Dis. Child. **43**: 655 (March) 1932	M	3 yr.	Left adrenal	Skull
Lightwood, R.: Proc. Roy. Soc. Med. **25**: 967 (May) 1932	M	3 yr. 5 mo.	?	Skull and long bones; no histologic report
Klein, J.: Am. J. M. Sc. **184**: 491 (Oct.) 1932	F	2½ yr.	Right adrenal	Mesenteric lymph nodes, skull, left humerus, ribs, liver, lungs, spleen, orbital fat
Law, F. W.: Lancet **2**: 1101 (Nov. 19) 1932	M	11 mo.	Left adrenal	Skull, liver, lungs, thoracic glands, lower pole of right kidney
Smith, J.: Lancet **2**: 1214 (Dec. 3) 1932	M	17 mo.	Right adrenal	Pancreas, abdominal glands, subcutaneous area
Tidswell, F., and Sear, H. R.: Australian & New Zealand J. Surg. **2**: 360 (April) 1933	M	6 yr.	Right adrenal	Skull, ribs, thorax
	F	3 yr.	Left adrenal	Skull, sternum, thorax
Sear, H. R.: Australian & New Zealand J. Surg. **2**: 370 (April) 1933	8 additional cases; diagnosis made by roentgen findings; not all verified by autopsy or biopsy			
Colville, H., and Willis, R. A.: Am. J. Path. **9**: 421 (July) 1933	F	8 yr.	Both adrenals	Right femur and spleen
Rupilius, K.: Ztschr. f. Kinderh. **55**: 708, 1933	M	4 yr.	Right adrenal	Skull, liver, pancreas, retroperitoneal glands and ribs
Blacklock, J. W. S.: J. Path. & Bact. **39**: 27, 1934	16 cases of adrenal neuroblastoma; diagnosis verified by autopsy or biopsy			
Meyer, H. S.: J. Pediat. **4**: 517 (April) 1934	M	3 yr.	Right adrenal	Ribs, iliac glands, long bones, skull; axillary, inguinal, cervical and (right) popliteal glands
McNamara, P.: Henneger, W. A., and Lytle, C. C.: J. Iowa M. Soc. **24**: 147 (March) 1934	F	3 yr.	Right adrenal	Vena cava and right kidney
	M	14 mo.	.....	.....
Van der Strateen and Maldague: Arch. d'opht. **50**: 513 (Aug.) 1933	F	3½ yr.	Left adrenal	Skull
	F	4 yr. 9 mo.	Left adrenal	Skull
	F	14 yr.	Right adrenal	Skull, bones, ovary
	M	11 mo.	Right adrenal	None
Burke, E. M.: Am. J. Cancer **20**: 338 (Feb.) 1934	M	2½ yr.	Right adrenal	Liver
Bustamente, G. B.: Arch. argent. de pediat. **5**: 384 (July) 1934	F	4 yr.	Right adrenal	Thoracic mediastinal and retroperitoneal lymph nodes
Peters, H. L., and Horn, B.: Am. J. M. Sc. **188**: 372 (Sept.) 1934	M	2 yr.	Right adrenal	Liver, retroperitoneal lymph glands
Nakatani, M.: Tr. Soc. path. jap. **24**: 581, 1934	F	2 yr. 5 mo.	Left adrenal	Retroperitoneal lymph nodes, skull, ribs, porta hepatis
	F	7 mo.	Left adrenal	None
	M	2 mo.	Right adrenal	Liver
	M	1½ mo.	Right adrenal	Mesenteric and retroperitoneal lymph nodes
	F	4 yr.	Right adrenal	Liver, retroperitoneal lymph nodes

TABLE 2.—*Data in Reported Cases of Adrenal Neuroblastoma—Continued*

Author	Sex	Age	Site	Metastases
Nakatani (continued)	M	89 days	Left adrenal	Liver
	M	10½ yr.	Right adrenal	Liver, porta hepatis; retroperitoneal mediastinal and tracheobronchial lymph nodes
	F	3½ mo.	Both adrenals	Liver
Eckardt, F.: Monatschr. f. Kinderh. **61**: 127, 1934	M	5 yr. 7 mo.	No autopsy	Skull and long bones; no histologic study
Neri, A.: Arch. ital. di anat. e istol. pat. **5**: 929 (Sept.-Oct.) 1934	?	5 mo.	Left adrenal	None ?
Mittelbach, M., and Szekely, P.: Frankfurt. Ztschr. f. Path. **47**: 517, 1935	M	2 mo.	Left adrenal	Liver
Askin, J. A., and Geschickter, C. F.: J. Pediat. **7**: 157 (Aug.) 1935	16 cases of adrenal neuroblastoma; diagnosis confirmed by autopsy or biopsy except in 1 case, in which metastases to bone were confirmed by roentgen study			
Lipset, A. H., and Glanzmann, E.: Kinderärztl. Praxis **6**: 417 (Oct.) 1935	F	6¼ yr.	Left adrenal	None
Wendel, W.: Zentralbl. f. Chir. **63**: 8 (Jan. 4) 1936	?	5 yr. 7 mo.	Left adrenal	None; operation but no autopsy
Gareiso, A.; Vergnolle, M. J., and Petre, A. J.: Rev. méd. latino-am. **21**: 31 (Oct.) 1935	M	11 yr.	Left adrenal	Hypophysis
LeFevre, W.: J. Michigan M. Soc. **35**: 94 (Feb.) 1936	M	4 yr.	Right adrenal	Lumbar vertebrae, ribs, skull and left os innominatum
Bonciu, C., and Dimitriu, O.: Rev. stiint. med. **24**: 1459 (Dec.) 1935	M	13 yr.	Right adrenal	?
Rinscheid, J.: Virchows Arch. f. path. Anat. **297**: 508, 1936	M	2½ yr.	Left adrenal	Liver; thoracic and supraclavicular lymph glands
	M	3¼ yr.	Left adrenal	Liver, left kidney, retroperitoneal lymph glands
	?	5¼ yr.	Left adrenal	Liver, pancreas, bones and retroperitoneal glands
	M	7 wk.	Right adrenal	Liver, intraperitoneal and retroperitoneal glands, cervical and axillary lymph glands
Stolz, J., and Kučerová, D.: Časop. lék. česk. **75**: 1148 (Sept. 11) 1936	F	10 mo.	Left adrenal	None
Hederstal, G.: Nord. med. tidskr. **12**: 1795 (Oct. 31) 1936	M	13 yr.	Both adrenals	Both kidneys
Lombard, P., and Montpellier, J.: Mém. Acad. de chir. **63**: 914 (June 30) 1937	M	3 yr.	Left adrenal	Liver and skin; alive 11 mo. after operation
Cust, N.: M. J. Australia **2**: 58 (July 10) 1937	F	4½ yr.	Right adrenal	Orbits and liver
Spreng, A.: Schweiz. med. Wchnschr. **66**: 1192 (Nov. 21) 1936	M	2 wk.	Left adrenal	Liver and skin
Rhea, L. J., and Mead, C. I.: J. Pediat. **10**: 37 (Jan.) 1937	F	5 yr.	Right adrenal	Cervical, mediastinal, retroperitoneal and inguinal glands, ribs, vertebrae, skull, femur and iliac bones
	F	3 yr.	Right adrenal	Liver and retroperitoneal glands
Stern, R. O., and Newns, G. H.: Arch. Dis. Childhood **12**: 267 (Oct.) 1937	19 cases of tumors of sympathetic nervous system of suprarenal origin; diagnosis confirmed by autopsy or biopsy			
Skellitel: Rev. méd. del Rosario **27**: 557 (July) 1937	M	7 yr.	Left adrenal	Bone
Bergstrom, V. W.: Am. J. Clin. Path. **7**: 516 (Nov.) 1937	F	Newborn: died aged 31 days	Both adrenals	Kidneys, spleen, lymph glands, skull, skin
Kato, K., and Wachter, H. E.: J. Pediat. **12**: 449 (April) 1938	M	2½ yr.	Right adrenal	Numerous bones, skull, liver, right kidney, lymph nodes
	F	2¼ yr.	Right adrenal	Liver, numerous bones, skull, retroperitoneal nodes

The examiner was inclined to make a diagnosis of nephritis with undetermined anemia, the transfusion having changed the original picture.

The liver remained large throughout the clinical course but usually was not tender. At no time could we make out any enlargement of the spleen; later we were able to detect a mass in the left upper part of the abdomen, but it was not smooth and regular like a spleen.

By October 22 severe pains had developed in the joints of the right knee, left ankle and left shoulder. These areas were extremely tender to manipulation. They were slightly hot but not inflamed. At this time the temperature went to 102 F. for a few days, but this was the only time it was elevated by more than 1 or 2 degrees.

Three days later there was an ecchymosis 3 cm. in diameter at the outer corner of the right eye.

Fig. 1.—Photograph of the patient, showing the proptosis of the right eye, the ecchymosis and the enlarged abdomen. (The stain over the abdomen is due to the solution of trinitrophenol used on the skin.)

On October 29 there was exophthalmos of the right eye; this persisted. On November 12, two weeks later exophthalmos or protrusion of the left eye appeared (fig. 1).

By this time we could feel the separation of the frontal sutures, which could readily be seen on the roentgen examination. By November 25, after many vacillations in making a diagnosis, we concluded that we were dealing with a neuroblastoma of the adrenal.

During the following two weeks the patient steadily lost ground. The anemia increased, and the child became greatly exhausted. She lost interest in her toys and surroundings and finally died. The only improvement derived from any medicine or procedure was the temporary benefit resulting from blood transfusions.

At times there appeared to be slight jaundice, but the icterus index was within normal limits.

Laboratory Examination.—During the eleven and one-half weeks of illness fifteen complete blood counts and four Schilling counts were made. The hemoglobin content was never above 69 per cent and it dropped as low as 49 per cent. The highest red cell count, made after the fifth transfusion, was 3,900,000. The number of cells dropped as low as 2,600,000. There was some poikilocytosis; anisocytosis and achromia were present. There were no nucleated red cells. The leukocyte count never rose above 8,000; the lowest count was 3,800. Differential counts showed polymorphonuclears ranging from 69 to 74 per cent and lymphocytes from 24 to 36 per cent. There were no juvenile cells or myelocytes; monocytes numbered 1 or 2 per cent, eosinophils 0, 1, or 2 per cent, basophils 1 per cent and reticulocytes 3 per cent. The platelet count was 230,000. In tests of fragility, hemolysis began with a 0.48 per cent solution and ended with a 0.42 per cent solution. The bleeding time was two and a half minutes and the coagulation time four and one-half minutes. The blood chemistry was normal throughout. The cholesterol content of the blood was 250 mg. per hundred cubic centimeters, of which the cholesterol esters comprised 109 mg. or 45 per cent. The serum contained 5.9 mg. of protein, of which 3.2 mg. was globulin and 2.7 mg. albumin.

Urinary examinations rather constantly showed a trace of albumin, with no blood or other changes except those already reported. Wassermann and Kahn reactions were negative on two occasions. The blood pressure was of no diagnostic help; usually it was about 90 systolic and 55 diastolic. On November 26 a spinal tap yielded 6 cc. of clear fluid, which was under a pressure of 62 mm. of mercury. There was 1 cell per cubic millimeter. Sugar was present and globulin absent. The Mantoux reaction was negative.

A biopsy of a left inguinal gland was made on November 8. Microscopic examination showed considerable proliferation of small lymphocytes. There were fairly large numbers of mononuclear cells and a considerable number of disintegrated red blood cells. No large multinuclear cells or eosinophils were seen. There was no evidence of a malignant process or of tuberculosis.

Marrow obtained by sternal puncture showed red cells only. There were no bone marrow cells. There were 18 per cent normoblasts, 8 per cent monocytes, 12 per cent lymphocytes, 26 per cent staff cells, 30 per cent neutrophils and 6 per cent eosinophils. A pyelogram gave negative findings or was not helpful. On November 1 the eyegrounds were reported to be normal. There was marked decrease of vision in the right eye. The child was given five transfusions, receiving 150 cc. of blood on September 30, 200 cc. on November 4, 200 cc. on November 6, 100 cc. on November 10, and 100 cc. on November 14.

On October 29 roentgen study of the chest showed a mediastinal shadow on the left, thought to be due to lymphadenopathy. A roentgenogram of the skull taken on November 15 showed separation of the frontal sutures but no punched-out areas of softening. There were striations between the inner and the outer plates (fig. 2*A*). The roentgenogram of the long bones showed periosteal elevation of the femur and of the humerus (fig. 2*B*).

Postmortem Examination.—Gross Study: The body was somewhat undernourished; there was marked pallor throughout. The right eye showed exophthalmos; there was subcuticular ecchymosis below it. In the right groin was a palpable inguinal gland. The entire abdomen was markedly distended. The region of the parotid and the cervical glands on the right showed palpable adenopathy. There was evidence of an incisional scar in the left inguinal region. No other evidence of external pathologic change or scar formation was noted. There was decided thinning of the hair of the head.

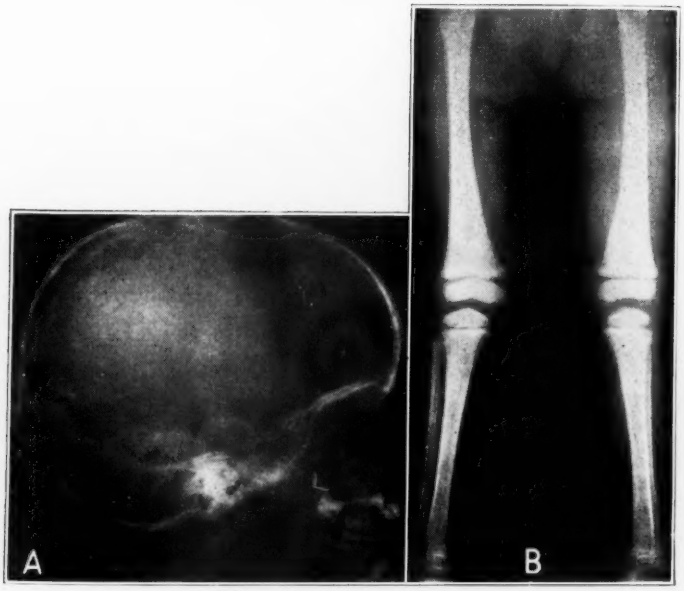

Fig. 2.—*A*, roentgenogram of the skull, showing separation of the frontal sutures and osteoporosis. *B*, roentgenogram of the long bones, showing periosteal elevation.

Fig. 3.—*A*, postmortem view of the abdominal cavity, showing the enlargement and mottling of the liver due to the metastases. *B*, the retroperitoneal mass, in which the right kidney is embedded. *C*, the right kidney and the overlying adrenal tumor.

The stomach and intestines were normally distended with gas. The liver was pale and enormously enlarged, the border extending to the umbilicus; there was minute whitish mottling throughout all lobes. The weight was 850 Gm. The gallbladder was normal. The spleen was normal in size, shape and color. The left kidney was pale, and the adrenal gland was atrophic and hard. The entire series of mesenteric and abdominal lymph nodes formed a mass involving the

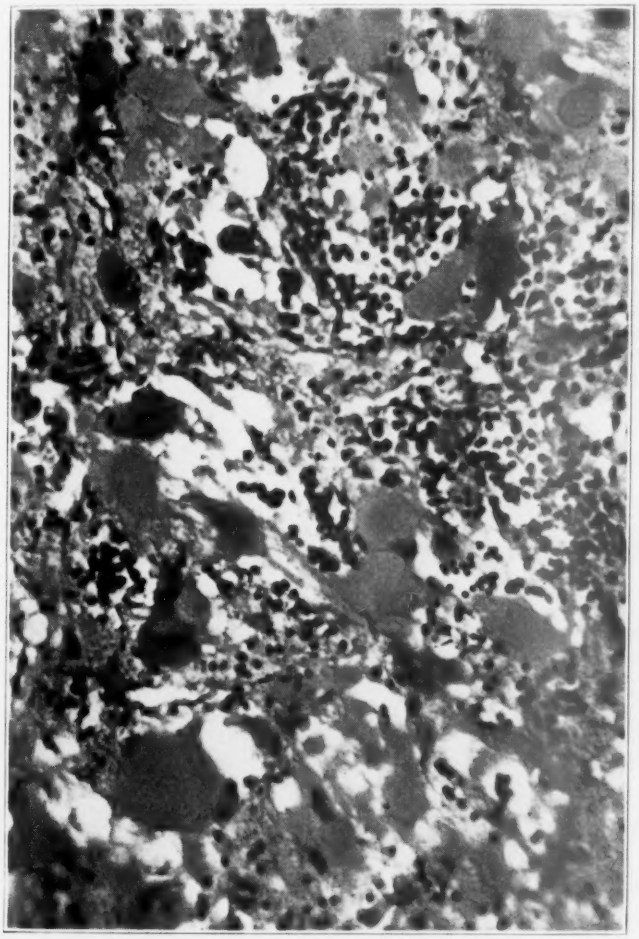

Fig. 4.—Section of the primary tumor, showing large neurocytes with prominent nucleoli, nerve fibers and small round cells (neuroblasts). Degeneration is marked throughout the entire tumor.

entire right kidney and adrenal gland and enveloping the pancreas; this consisted of glandular nodules varying from ½ inch (1.27 cm.) to 5 inches (12.7 cm.) in diameter. The mass, including the right kidney weighed 878 Gm. and measured about 12 by 15 by 7 inches (30 by 38 by 18 cm.). A large mass, 3 inches (8 cm.) in diameter, in the lower left part of the pelvic region was connected with the larger mass in the abdominal cavity. Most of these glands on section appeared

red and hemorrhagic. The tumor mass, as measured in the region of the right adrenal body, at the upper pole of the right kidney but separated from it, was about 3 inches in diameter; on section it appeared yellow and hemorrhagic. The fallopian tubes, ovaries and uterus were apparently normal. The bladder, which was distended with urine, was normal. The appendix was normal. There was a moderate amount of free fluid in the abdominal cavity (fig. 3).

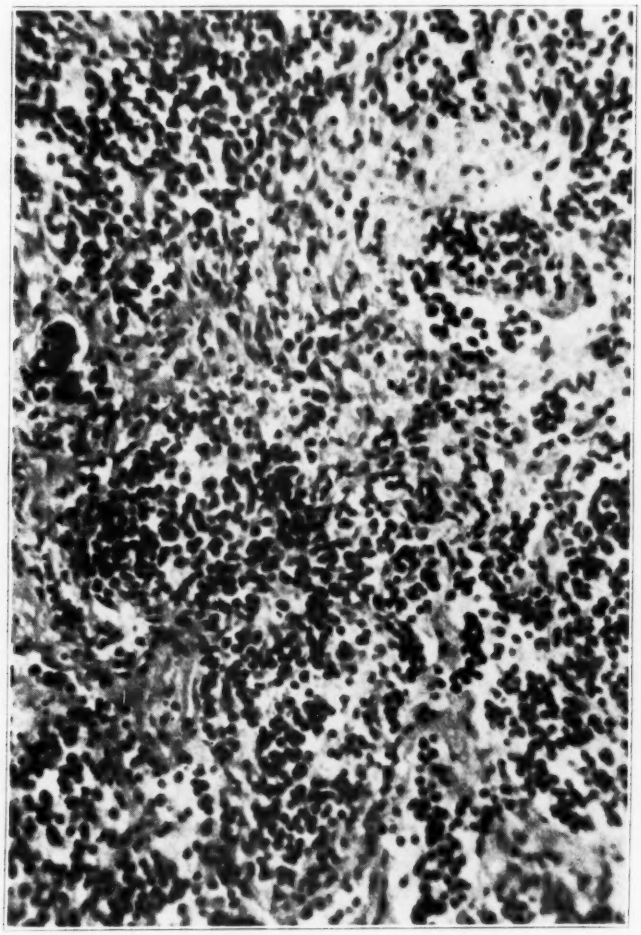

Fig. 5.—Section through the liver showing a metastatic nodule of small round cells (neuroblasts), which have a tendency to arrangement in columns along bands of fine fibrillar network.

The diaphragmatic pleura on the right showed a few enlarged lymph glands, and numbers of enlarged mediastinal lymph glands; the pleural cavity contained a moderate amount of fluid. The right and the left main bronchus and their branches were involved with enlarged lymph glands. In the area of the thymus, a mass 5 cm. in diameter showed multiple metastatic nodules. In the pericardium was a small amount of free fluid. The heart was normal. The anterior thoracic

portion of the spine showed enlarged lymphatic nodules along the transverse processes. The sternum was slightly adherent to the mass of glands in the region of the thymus. The bony structure of the chest wall did not seem to be invaded. Permission for examination of the head, the brain and the remainder of the nervous system was not granted.

The right kidney was pale, and the apexes of the renal pyramids had a grayish yellow appearance suggestive of the yellowish colony of the adrenal tumor.

Microscopic Study: Sections of the right adrenal (primary tumor) showed widespread degeneration, but enough of the structural features remained to indicate that the entire tumor, as contained in several large sections, had the same pattern. Nerve cells, which were arranged singly or in groups, were scattered in or surrounded by stroma that contained many nerve fibers. The neurocytes were unmistakable; many cells showed considerable differentiation, with an achromatic nucleus, a large and chromatic nucleolus and short eosinophilic processes.

One section showed the adrenal gland external to the tumor; this suggested that the tumor originated just outside of the adrenal proper. At one pole of this adrenal the medulla was replaced by uniform small oval cells with an irregular central fibrillar area similar to the cells in the metastases (fig. 4).

The left adrenal tumor was dense and well preserved; it consisted of densely packed bundles of cells of neuromatous nature in which were islands or groups of cytons.

The tumorous deposits in the organs sectioned, the liver, lung and the kidney, had an entirely different makeup. The cells were uniform, with a small oval nucleus that contained finely scattered chromatin material, had no large nucleolus and was surrounded with scanty cytoplasm which occasionally had small pointed projections. They were arranged chiefly in dense masses and groups but in some places were arranged around irregular eosinophilic bandlike areas that had a fine granular or fibrillar appearance. This was not really a pseudorosette formation but did suggest an abortive attempt to produce it (fig. 5).

The left kidney, left adrenal, right ovary, heart and spleen did not manifest secondary involvement.

Diagnosis: This was a widespread neuroblastoma of the adrenal; the primary tumor showed ganglioneuromatous as well as true neuroblastomatous formation.

In the metastases only the neuroblasts were evident. The immediate cause of death was the neuroblastoma of the right adrenal. A contributory cause was secondary metastatic involvement of the liver, the right kidney, the pancreas and the abdominal and mediastinal glands.

COMMENT

We believe that in the present case the growth was a true neuroblastoma of the incompletely differentiated type. It is interesting to note that the original tumor contained comparatively mature cells, the large neurocytes, as well as neuroblasts, which were shown as small round cells. However, the metastases showed only the neuroblasts. This is easily understandable because mature cells constitute a benign element which does not metastasize, while neuroblasts metastasize widely.

This tumor can be classified as belonging to the Hutchinson type, since pronounced involvement of the skull was present. Notwithstand-

ing this, there was also extensive involvement of the liver. This brings out very clearly the fact that these two classifications are arbitrary.

The symptoms and results of examination in our case were typical. In reference to the inverted albumin-globulin ratio of the serum, we have felt that the reduced albumin value was due to the damage caused in the liver by the extensive metastatic nodules. It has been shown [18] that with chronic hepatic lesions of an advanced type there is a moderate reduction in the value of the serum protein. This diminution occurs chiefly in the albumin fraction.

CONCLUSIONS

A review of the literature reveals that 113 cases of adrenal neuroblastoma in infants and children have been reported since the review of Scott, Oliver and Oliver.

The average age in this series was $3\frac{1}{12}$ years, while the average age of children with tumors of the Pepper type alone was $1\frac{1}{2}$ years.

The division of such tumors into the Pepper and the Hutchinson type is helpful, but the delineations are rather arbitrary.

Judging by the number of cases reported in the literature, suprarenal neuroblastoma is still comparatively rare.

The clinical picture is governed largely by the metastases, and the outcome is almost invariably fatal within a few months after the onset of the symptoms.

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18. Myers, W. K., and Keefer, C. S.: Relation of Plasma Protein to Ascites and Edema in Cirrhosis of the Liver, Arch. Int. Med. **55**:349 (March) 1935.

News and Comment

GENERAL

Children's Hospital Research Foundation.—Announcement is made by Dr. A. Graeme Mitchell, director of the Children's Hospital Research Foundation, Cincinnati, and Dr. Glenn E. Cullen, director of laboratories, that on authorization of the board of trustees a scientific advisory council has been appointed. This consists of Dr. O. T. Avery, member of the Hospital of the Rockefeller Institute for Medical Research; Dr. Ernest Goodpasture, professor of pathology, Vanderbilt University School of Medicine; Dr. A. Baird Hastings, professor of biological chemistry, Harvard University Medical School, and Dr. A. N. Richards, professor of pharmacology, University of Pennsylvania School of Medicine. The second meeting of this Council was held in Cincinnati on Sept. 28 and 29, 1938.

The Children's Hospital Research Foundation was created in 1929 through the generosity of Mr. William Cooper Proctor. Its facilities include its own laboratory building and affiliations with the Children's Hospital of Cincinnati, the pediatric department and the contagious disease pavilions of the Cincinnati General Hospital, the Children's Convalescent Home, the Babies' Milk Fund Association and the Ohio Soldiers' and Sailors' Orphans' Home at Xenia, Ohio. The Children's Hospital and its Research Foundation are affiliated by agreement with the University of Cincinnati, the professor of pediatrics in the university being the director of the medical service and the director of the foundation. Approximately one hundred and fifty publications have appeared from the Research Foundation. At present additions to the staff and certain new lines of investigation are contemplated.

American Board of Pediatrics.—The American Board of Pediatrics will hold examinations during 1939 as follows: on Wednesday, April 26, in New York (appointments for this examination must be made before Dec. 26, 1938); on Tuesday, May 16, in St. Louis, during the meeting of the American Medical Association (appointments for this examination must be made before Jan. 16, 1939), and on Tuesday and Wednesday, November 14 and 15, in Cincinnati, preceding the annual meeting of the American Academy of Pediatrics (appointments for this examination must be made before July 14, 1939).

Meeting of Pediatric Section.—The Pediatric Section of the American Medical Association will have headquarters in Hotel Chase for the meeting in St. Louis on May 15 to 19, 1939. It is suggested that those expecting to attend the meeting make reservations early. Rates are as follows: single rooms from $3, double rooms from $4 and twin bed double rooms from $5. For reservations address John Reinhardt, American Medical Association Housing Bureau, 910 Syndicate Trust Building, St. Louis.

UNIVERSITY NEWS

Dr. Rolf R. Struthers has been appointed professor of pediatrics at McGill University and physician in chief at the Children's Memorial Hospital in Montreal, Canada, to succeed Dr. H. B. Cushing, who becomes emeritus professor of pediatrics and honorary physician in chief.

DEATHS

Dr. Erich Peiper, professor of pediatrics at Greifswald, died recently. Professor Peiper was one of the pioneers of pediatrics in Germany.

Obituaries

CLARENCE A. EARLE, M.D.

1862—1938

On October 29 Dr. Clarence A. Earle, of Des Plaines, Ill., died of cerebral hemorrhage.

Dr. Earle was a pioneer in the Middle West in immunization against diphtheria and scarlet fever. His zeal in this field was most commendable because the work was carried out under such difficulties. He had the respect of all who knew him, and pediatrics has lost an active representative.

Abstracts from Current Literature

Biochemistry; Bacteriology, and Pathology

Hemolytic Streptococci of Human Feces. F. R. Smith and J. M. Sherman, J. Infect. Dis. **62**:186 (March-April) 1938.

A study was made of 109 cultures of hemolytic streptococci isolated from 45 samples of feces from normal persons. The organisms were identified by means of the Lancefield precipitin technic and by physiologic tests.

The most common hemolytic streptococcus of the human intestine is Streptococcus zymogenes, a member of the Lanceford group D, and the second in frequency is the related "enterococcus," Streptococcus durans, also a member of group D.

The other hemolytic streptococci found were members of the Lancefield groups B (Streptococcus mastitidis), C (human type), F ("minute hemolytic streptococcus") and G (Streptococcus anginosus and related types).

Toomey, Cleveland.

Serums, Antitoxins, and Drugs in the Treatment of Meningococcus Meningitis. S. E. Branham, Pub. Health Rep. **53**:645 (April 29) 1938.

After a critical review of the subject Branham concludes that it is becoming more and more evident that it is necessary to use cultures of meningococci which are good antigens in order to make good serums. Just how such strains are to be chosen is a subject of much study at the present time. It seems likely that certain drugs may prove to be useful adjuncts to serum in treating meningococcic infections.

Sanford, Chicago.

Effect of Supersonic Waves on Tetanus Toxin. H. Kakusui and S. S. Nan, Acta pædiat. japon. **44**:279 (Feb.) 1938.

When supersonic waves (0.2 ampere, 450 kilocycles per second) are applied to tetanus toxin in dry form for three minutes there occurs a diminution of both tetanospasm and tetanolysin.

Kato, Chicago.

Metabolism; Infant Feeding; Milk and Other Foods

Hemolytic Streptococci of Milk. J. M. Sherman and C. F. Niven, J. Infect. Dis. **62**:190 (March-April) 1938.

A total of 313 samples of commercial milk (68 raw and 245 pasteurized) were examined for hemolytic streptococci. Narrow zone hemolytic types in blood agar, the most representative of Streptococcus mastitidis, were not considered. Only 8.5 per cent of the pasteurized samples contained hemolytic streptococci, whereas broad zone hemolytic types were obtained from 18 per cent of the raw samples.

The cultures isolated were studied serologically and physiologically, and on the basis of these results 6 groups or species were recognized: Streptococcus mastitidis (Lancefield group B), the "animal pyogenes" (Lancefield group C), Streptococcus durans (Lancefield group D), Streptococcus zymogenes (Lancefield group D) and two other types which differ serologically and physiologically from any adequately described species of streptococcus.

The prevailing types of hemolytic streptococci in raw milk are Streptococcus mastitidis and the "animal pyogenes"; the most common forms in pasteurized milk are Streptococcus durans and Streptococcus zymogenes.

Toomey, Cleveland.

METABOLISM STUDIES ON AGE DISPOSITION TO KETOSIS IN HUMAN BEINGS. W. HEYMANN, J. Pediat. **12**:21 (Jan.) 1938.

Thirty-six subjects from 1 month to 35 years of age were placed for three consecutive days on a ketogenic diet having a ratio of 2.5 : 1. Daily determinations were made of the acetone excreted in the urine. Ketonuria was found to be minimal up to the age of from 7 to 8 months. From then on it was found to increase during the first four years of life, reaching a broad peak at from the fourth to the eighth year and decreasing during prepuberty, when values equal to those found in adults were obtained, values which were much higher than those found in infants.

When acetone or sodium acetoacetate was fed to healthy infants and children under normal nutritional conditions, no quantitative difference in ketonuria was found. Heymann concludes that the variation in disposition to ketosis with age has to be explained by a difference in the ability to produce acetone bodies rather than by a difference in the ability to utilize, destroy or excrete them. He believes that these results substantiate the assumption that in healthy infants the liver retains glycogen more tenaciously than it does in healthy children. A deviation from this physiologic equilibrium might explain the occurrence of glycogen storage disease and steatosis of the liver in infancy and childhood. The increase in the disposition to ketosis with increase in age can also possibly be explained by the assumption that the infantile pituitary gland produces the ketogenic principle to a lesser extent than does the pituitary gland of the child.

RAUH, Cincinnati. [FROM THE AUTHOR'S SUMMARY].

DIAGNOSIS AND TREATMENT OF OBESITY IN CHILDREN. J. H. HESS and R. H. KUNSTADTER, M. Clin. North America **22**:161 (Jan.) 1938.

Two types of obesity are encountered in children: exogenous, due to hyperalimentation, and endogenous, the result of abnormal metabolism. The latter type is discussed more fully in this paper. Of the various factors which are responsible for metabolic aberration—the heredity, the constitution, the nervous system and the endocrine glands—the last are the most important. In the majority of cases obesity in childhood outside of simple hyperalimentary overweight arises from hypofunction or dysfunction of the thyroid gland or of the hypophysis or of both. Recent studies, however, tend in certain cases to incriminate also the nuclei in the hypothalamic region independent of the hypophysis. The intimate physiologic relationship between the thyroid gland and the hypophysis makes difficult a determination of the role which each gland plays in the genesis of obesity. The retarded growth characteristic of hypothyroidism in children may result from deficiency of the growth-stimulating factor of the pituitary gland, while hypofunction of the latter may bring about secondary hypothyroidism due to diminished secretion of the thyroid-stimulating hormone. From a therapeutic standpoint, however, it is important to determine the gland which is primarily at fault.

Hypothyroidism in the young child may manifest itself by the usual and obvious signs and symptoms of this disorder or may occur in such a mild or masked form as to escape detection unless a careful analysis of the history, physical signs and response to therapy establishes the diagnosis.

In the present state of knowledge of the physiology of the pituitary gland it is not possible to correlate fully clinical findings with the underlying pathologic changes. However, it is possible to distinguish the following types of pituitary obesity: (1) basophilic adenoma of the pituitary (Cushing's syndrome), due to hypersecretion of the basophilic cells and probably to associated changes in the gonads and the adrenal cortex; (2) dystrophy adiposogenitalis (Fröhlich's syndrome), involving the anterior and intermediary (posterior) lobes of the pituitary and probably the adjacent structures of the hypothalamic region; (3) mixed thyroid and pituitary disturbances. Other types of obesity due to dysfunction of other glands—the gonads, the adrenals and the pancreas—occur rarely in childhood.

Irrespective of the underlying cause of the obesity, dietary restriction is the most important mode of treatment. A diet high in protein and low in calories is of decided value and should furnish the child at least from 2 to 2.5 Gm. of protein per kilogram of body weight. Temporary restriction of fluids to from 800 to 1,000 cc. daily is helpful. Sufficient dehydration usually results when a diet high in protein is maintained. Endocrine therapy is definitely beneficial in certain types of obesity. Thyroid substance, an extract of the whole anterior lobe of the pituitary and gonadotropic substances, alone or in combination, are valuable agents when used intelligently.

EUGENE H. SMITH, Ogden, Utah.

NUTRITION AND NUTRITIONAL DISEASES. L. G. PARSONS, Lancet **1**:65 (Jan. 8) 1938.

These two Withering Lectures do not lend themselves to abstracting but are well worth reading in the original. Among the topics considered are: the absence of any definite standards of nutrition; the diseases of the erythron; iron deficiency; thyroxin and vitamin C.

LANGMANN, New York.

CREATINE RETENTION IN BLOOD AND CEREBRO-SPINAL FLUID. A. BOLLIGER and A. L. CARRODUS, M. J. Australia **1**:69 (Jan. 8) 1938.

Bolliger and Carrodus found the creatine content in the cerebrospinal fluid and blood plasma of normal persons to vary from 0.2 to 0.4 mg. per hundred cubic centimeters of fluid; that in their blood cells, from 2.6 to 4.2 mg. per hundred cubic centimeters of blood. Specimens of cerebrospinal fluid obtained post mortem exhibit a sharp rise in creatine content. Creatine retention occurs in cerebrospinal fluid, in blood plasma and in blood cells of nephritic persons but not to an extent which would warrant its estimation for diagnostic and prgnostic purposes in preference to determinations of creatinine.

GONCE, Madison, Wis.

MAGNESIUM AND CARBOHYDRATE METABOLISM. A. B. CORKILL and A. H. ENNOR, M. J. Australia **1**:113 (Jan. 15) 1938.

Corkill and Ennor report that magnesium chloride administered by slow intravenous infusion to young and semiadult rabbits, contrary to the report of Franke, results in no accumulation of glycogen in the liver. Such an experiment, however, does result in definite hyperglycemia. The latter action of magnesium is dependent on the adrenal glands, since it does not occur in adrenalectomized animals.

GONCE, Madison, Wis.

BLOOD UREA CLEARANCE TESTS. G. A. PENINGTON, M. J. Australia **1**:163 (Jan. 22) 1938.

Some of the shortcomings of the usual blood urea clearance test are briefly discussed, and an indication is given of the enhanced value of the test after a urea meal is given. A new technic is given for making the test after the urea meal, with reasons for the use of the values thus obtained. A line chart for the determination of the blood urea clearance in percentage of normal is provided.

GONCE, Madison, Wis.

A CASE OF LEVULOSURIA IN A CHILD. G. PAISSEAU, J. FERROIR and A. MANGEOT, Arch. de méd. d. enf. **41**:5 (Jan.) 1938.

An instance of this rare disturbance in carbohydrate metabolism is reported in a boy aged 5. Since but 30 cases have been described, the writers outline in considerable detail not only the findings in the case under discussion but the requirements for diagnosis. Among these may be noted:

1. The urine must reduce Fehling's solution, but this is a property possessed by the pentoses and other sugars as well as by substances not identified with the carbohydrates.

2. It must show a rotatory power toward the left, but this also is a characteristic of other sugars and of derivatives of betaoxybutyric acid and of glycuronic acid.

3. The amounts employed for reduction and for polarization should be in accordance.

4. It must be fermentable, to eliminate the pentoses.

5. It must give a red coloration in the presence of resorcinol and sulfuric acid, to differentiate it from dextrose.

AMESSE, Denver.

THE USEFULNESS AND THE POSSIBILITY OF CREATING DEPOTS FOR THE COLLECTION OF HUMAN MILK. D. MOGGI, Lattante **9**:86 (Feb.) 1938.

On the basis of the experience of the last five years in the pediatric clinic at Florence, Italy, Moggi has outlined an ideal organization for collecting and dispensing human milk.

HIGGINS, Boston.

THIEMIA IN CHILDREN: I. THE METABOLISM OF SULFUR. I. BIDDAU, Riv. di clin. pediat. **36**:1 (Jan.) 1938.

Biddau summarizes present knowledge of the biochemistry and the metabolism of sulfur.

HIGGINS, Boston.

ARAKAWA'S REACTION AND CELL CONTENT OF HUMAN MILK. A. SATO and T. SUZUKI, Tohoku J. Exper. Med. **32**:84 (Jan. 30) 1938.

A sample of human milk is said to give an Arakawa reaction when it becomes blue on the addition of Arakawa's reagent. The chemical formula of this reagent is not given in this paper. In trying to determine various factors which may be responsible for producing a milk that reacts with the Arakawa reagent, the authors studied the copper peroxidase reaction of the cells of human milk. They found that human milk giving the Arakawa reaction had a considerably higher content of peroxidase-positive cells than milk which was negative to the Arakawa reagent.

LESLIE, Evanston, Ill.

Newborn

BLOOD SUGAR DURING LABOR, AT DELIVERY AND POSTPARTUM, WITH OBSERVATIONS ON NEWBORNS. R. C. KETTERINGHAM and B. R. AUSTIN, Am. J. M. Sc. **195**:318 (March) 1938.

The authors show that the Jeghers-Myers modification of the Folin-Malmros micromethod for determining blood sugar is an accurate and practical test for use with adults and newborn infants. Eighty-five per cent of the duplicates check within 3 per cent.

The mean value for the maternal blood sugar at delivery in 50 cases was 124.6 mg. per hundred cubic centimeters of blood, with the values in 60 per cent of the cases falling between 110 and 140 mg., which is approximately 40 to 50 mg. above the normal range.

The mean value for the blood sugar of 47 infants at birth was 103.6 mg.; 94 per cent of these infants presented values lower than those of their respective mothers.

Both anesthesia and labor have been shown to contribute to the rise in blood sugar at delivery, but there is no indication that the duration of these factors is the primary cause of the rise.

The authors have established the normal range of the blood sugar for newborn infants by the modified Folin-Malmros technic. During the first two days of life the blood sugar ranges from 55 to 75 mg. per hundred cubic centimeters, with slightly higher values on the third day. Within from three to six hours after birth the blood sugar drops to the normal range for infants.

HENSKE, Omaha.

EPIDEMIC DIARRHEA OF THE NEW-BORN: III. EPIDEMIOLOGY OF OUTBREAKS OF HIGHLY FATAL DIARRHEA AMONG NEW-BORN BABIES IN HOSPITAL NURSERIES. S. FRANT and H. ABRAMSON, Am. J. Pub. Health **28**:36 (Jan.) 1938.

Frant and Abramson call attention to a chain of outbreaks of highly fatal diarrhea in newborn infants during the period of the customary care of such infants in hospital nurseries in the past three years. During this period in 15.5 per cent of 4,594 babies born in the hospitals of New York the disease developed with a mortality of 7.3 per cent for the group and of 47 per cent for those who contracted the disease. Study of New York records shows that there has been a satisfactory reduction in death rates from all causes among infants from 1 month to 1 year of age but that the rate in the neonatal period has not been lowered. The number of deaths from diarrheal disease of the newborn has actually increased.

Bacteriologic studies of the various outbreaks revealed no source of the infection, and virus studies and autopsies likewise failed to clarify the problem. The authors point out the need for closer scrutiny of present medical and nursing care of newborn infants. Suggested technics have been reported by them elsewhere. Diarrheal disease of the newborn occurring in hospitals has been made a reportable disease in New York.

LIMPER, Louisville, Ky.

NODULAR GOITER OF THE NEWBORN WITH SUBSEQUENT ADENOCARCINOMA. G. A. STEVENS and W. W. WAITE, J. A. M. A. **110**:803 (March 12) 1938.

A child had a goiter present from birth, unchanged in size. This was removed at 7 years of age. The nodule contained malignant tissue. The patient did not live in a goiter belt, and there were no relatives with goiter. Malignant changes were probably present but not extensive, since a two year recovery is recorded.

HEERSMA, Kalamazoo, Mich.

BLOOD COAGULATION FACTORS IN HEMORRHAGIC DISEASE OF THE NEWBORN AND THE VALUE OF INTRAMUSCULAR INJECTIONS OF FATHER'S AND MOTHER'S BLOOD. H. N. SANFORD and E. I. LESLIE, J. Pediat. **12**:16 (Jan.) 1938.

Sanford and Leslie studied blood coagulation in 2 cases of hemorrhagic disease of the newborn. In both cases they found the number of plasma platelets to be normal. In both cases the coagulation time for natural venous plasma was increased in comparison with that of normal newborn babies. The coagulation time of platelet-free plasma was also markedly increased, as was the coagulation time of plasma containing a platelet concentrate. They believe that the failure of the blood to coagulate lies in a qualitative dysfunction of the platelets, in an inability of the platelets to disintegrate normally, and that this may be an exaggeration of the increased resistance of the platelets found in the blood of the normal newborn infant in the first three days of life. An intramuscular injection of blood was used in the treatment of a baby on the third day, and the coagulation time of the plasma returned to normal by the seventh day. Studies were carried out to determine the effect on the plasma coagulation time of the blood of 20 normal babies of intramuscular injection of father's and mother's blood. In all cases the coagulation time on the day after the injection was increased, more so after the injection of mother's than after that of father's blood. Because of these results no treatment was given in the second case of hemorrhagic disease, and the coagulation factors were observed. The coagulation time increased enormously on the third day, lessened on the fourth and was back to normal on the sixth. Clinically, the hemorrhage ceased spontaneously on the third day, and the infant's condition was good on the fourth day. The observations were identical with those found in the infant treated with an intramuscular injection of blood.

RAUH, Cincinnati.

MATERNAL NUTRITION AND NEONATAL DEATHS: A COMPARISON OF THE NEONATAL MORTALITY RATES OF QUEENSLAND AND SOUTH AUSTRALIA. A. J. TURNER, M. J. Australia **1**:490 (March 12) 1938.

The infant mortality rate in Queensland, Australia, in 1936 was 36.2. Of the deaths during the first year, 72 per cent were due to antenatal causes (premature birth, congenital weakness, malformation, birth injury, disease peculiar to the neonatal period). Of the deaths during the first month in the period from 1934 to 1936, inclusive, 86 per cent occurred during the first week of life, and these were all due to what have been classified as antenatal causes.

The infant mortality rates in Queensland and South Australia used to be equal, but since 1931 the rate in the latter state has been lower, especially in the year 1936—34.1, compared with 39.4. The explanation for this difference is found in a comparison of neonatal rates, that of Queensland in 1936 being 26.3 and that of South Australia being only 20.8.

This difference in the neonatal rates between the two states is explained by Turner on a nutritional basis. In Queensland the most important cause of malnutrition among women is the great deficiency of milk in their diet; especially is this the case among the unemployed and those living in the edge of subsistence. On the other hand, the South Australian government during the early years of the depression adopted the policy of supplying milk rations to the families of the unemployed, and since 1935 there have been issued one and a half pints of milk (709 cc.) in addition to other rations to every woman who produces a medical certificate that she is pregnant and needs the milk. GONCE, Madison, Wis.

INFLUENCE OF EUGENICS ON THE NATAL AND NEONATAL MORTALITY. A. MUGGIA, Lattante **9**:17 (Jan.) 1938.

It is necessary that prospective mothers who are syphilitic be given treatment if natal or neonatal mortality is to be diminished.

An example of improved health service is seen among the workers of the Royal Tobacco Factory in Turin, Italy. Tobacco has long been recognized as having a noxious influence on the uterus and ovaries, so that abortions and prematurity are frequent, and the infants small and of poor resistance. Under more rigid hygienic control the number of live births has increased and the number of abortions diminished. HIGGINS, Boston.

Acute Contagious Diseases

ELECTROCARDIOGRAPHIC CHANGES AND PERIPHERAL NERVE PALSIES IN TOXIC DIPHTHERIA. E. A. BURKHARDT, C. EGGLESTON and L. W. SMITH, Am. J. M. Sc. **195**:301 (March) 1938.

Serial electrocardiograms were made for 140 patients showing evidence of toxic diphtheria; in 28 cases the serial electrocardiograms showed changes of contour.

In 23 cases the T wave changes occurred between the fifth and thirty-ninth days of illness. The majority of changes occurred between the eighth and fifteenth days of illness.

In 17 cases conduction changes were shown between the fifth and the thirteenth day of illness. In 11 of these cases atrioventricular dissociation developed, and this complication invariably proved fatal.

Fourteen patients showing electrocardiographic changes died of toxic diphtheria. Seven of these received large doses of diphtheria antitoxin on or before the fourth day of illness. Early administration of antitoxin did not save this group of patients.

Peripheral nerve palsies occurred in 65 per cent of the patients presenting electrocardiographic changes. The paralysis apparently bore no causal relationship to the cardiac phenomena.

The essential histologic changes in the myocardium due to toxic diphtheria are shown to be progressively edema, congestion, cellular infiltration, degenerative changes in the muscle fibers and ultimately fibrosis.

The electrocardiographic findings constitute an important guide in the treatment of diphtheria. Complete inactivity is recommended for the patient whose serial electrocardiograms show abnormalities, until the conditions represented in the electrocardiograms have had ample opportunity to return to normal.

HENSKE, Omaha.

FAMILIAL AGGREGATION OF INFECTIOUS DISEASES. W. FROST, Am. J. Pub. Health **28**:7 (Jan.) 1938.

Frost reviews the work of Chaplin in the latter's study of the household as an epidemiologic unit and the latter's evaluation of the rate of secondary attack as a means of studying communicable diseases. We are indebted to Chaplin for the most extensive data available on scarlet fever, diphtheria and measles and even more for devising a method of assembling the necessary data for studying communicable diseases.

LIMPER, Louisville, Ky.

INCIDENCE OF POLIOCIDAL SERA IN REGIONS WHERE POLIOMYELITIS EPIDEMICS ARE INFREQUENT. N. P. HUDSON and E. TENNETTE, Am. J. Trop. Med. **18**:35 (Jan.) 1938.

Hudson and Tennette attempted by examining serum for neutralizing bodies to find some area in the world where poliomyelitis did not exist. Failing in this they studied serum from residents in two tropical sites and found that most of these contained the poliomyelitis neutralizing substances in their serum though the disease occurred only infrequently, and rarely in epidemic form. They concluded that there is a wide distribution of the virus and the disease, a general immunization of the residents to the virus and an effect of warm climate on the occurrence of epidemics.

BURPEE, Augusta, Ga.

PROBLEMS BEARING ON THE PATHOGENESIS AND TREATMENT OF ACUTE POLIOMYELITIS. P. H. HARMON, W. M. KRIGSTEN and H. N. HARKINS, Illinois M. J. **73**:195 (March) 1938.

From a review of the literature and their personal studies the authors conclude that some evidence has accumulated in a recent epidemic of poliomyelitis that points to the intestinal tract as the site of entry of the virus. Much of the evidence pertaining to the nasopharyngeal portal of entry has been obtained by animal experimentation and does not necessarily apply to the disease in man.

There are many factors that complicate the isolation of the virus of poliomyelitis from man. Among these may be cited the necessary use of an experimental animal, the presence of virus-neutralizing substances in the blood, nasopharynx and intestine, and the existence of different strains of virus.

There is no adequate preventive of the disease. The use of serum is scientifically sound, but the practical value of it has not been established. Chemical blockage of the nasopharyngeal area, while adequate in the laboratory, has likewise not been established as of value for man. More study of these and of other methods is needed.

The best results in the treatment of the acute disease have been obtained by the combination of early diagnosis, administration of massive doses of human convalescent serum and early prolonged and intelligent orthopedic supervision. Aids in dealing with the bulbar type of disease are absolute rest, agents to dehydrate the nervous system and the respirator.

BARBOUR, Peoria, Ill.

SCARLET FEVER IMMUNIZATION BY INTRACUTANEOUS INJECTION OF SCARLATINAL STREPTOCOCCUS TOXIN. R. A. KERN, J. CRUMP, R. L. RODDY and S. BOROW, J. Allergy **9**:125 (Jan.) 1938.

The article contains a number of interesting findings which are difficult to record in an abstract. The important ones are: Immunization can be produced by weekly intracutaneous injection of 0.1 cc. of scarlatinal streptococcus toxin. The immunity is obtained quickly and is of short duration. There is freedom from general reactions.

In the discussion following the reading of the paper it was suggested that the immunity might last longer if after some immunity had been established by two or three intracutaneous injections subsequent injections were made subcutaneously and larger doses employed. In this the authors concurred, since general reactions seem to occur less frequently following subcutaneous injections if some immunity has been established.

HOYER, Cincinnati.

TREATMENT OF PERTUSSIS WITH AN INTRANASAL SPECIFIC ANTIGEN. H. A. SLESINGER, Pennsylvania M. J. **41**:485 (March) 1938.

The intranasal method of administering pertussis antigen appeals to Slesinger for three reasons: 1. It eliminates the necessity of using the hypodermic needle, to which children and parents frequently object. 2. It can be administered easily by the mother. 3. There is complete freedom from reactions.

The method of administering is as follows: The patient is placed in a recumbent posture with the head hyperextended in a position below the level of the body. Ten drops of the antigen is then slowly instilled into each nostril, care being taken that the drops reach the level of the middle and superior turbinates. The patient is then kept in this position for from three to five minutes in order to facilitate absorption. Treatments were given every day or every second day for a total of from 4 to 12 doses, depending on the severity of the case and the type of response to treatment.

The specific soluble pertussis antigen was used intranasally in the treatment of 61 children with whooping cough. Marked improvement was shown in 49.2 per cent. The number and severity of the paroxysms were diminished, and the total duration of the illness was considerably decreased. Moderate improvement was shown in 26.2 per cent. Little or no improvement was shown in 24.6 per cent.

The antigen is of some value in the prevention of whooping cough in contacts. This prophylaxis is probably temporary.

LOGUE, Williamsport, Pa.

SUMMARY OF CURRENT PREVALENCE OF COMMUNICABLE DISEASES. Pub. Health Rep. **53**:69 (Jan. 21) 1938.

For the period of Dec. 5, 1937, to Jan. 1, 1938, 32,813 cases of measles were reported. This was almost five times the number reported in 1936 for the same period. This increase was in the Middle Atlantic, West and East North Central and East South Central regions. Scarlet fever with 18,928 cases was only slightly in excess, as was influenza. Meningococcic meningitis was slightly increased. Poliomyelitis, diphtheria and typhoid fever were below the median prevalence. The mortality from all causes was 12.2 per thousand, which is average for a four year period.

SANFORD, Chicago.

PREVALENCE OF COMMUNICABLE DISEASES IN THE UNITED STATES. Pub. Health Rep. **53**:405 (March 18) 1938.

For the period of Jan. 20 to Feb. 26, 1938, with the exception of New England and the Pacific Coast, measles is greatly in excess. At present the incidence equals that in the two years of greatest incidence, 1934 and 1935, and will probably go higher as the season advances. Smallpox, with 4,100 cases, is the highest since 1931. Poliomyelitis is 10 per cent in excess, as is typhoid fever. The rise in the

latter is due to a large number of cases in Louisiana and Texas. Scarlet fever, diphtheria, meningitis and influenza are below the average. The average mortality from all causes was 12 per thousand. This is the lowest for this period for the last thirteen years.

SANFORD, Chicago.

HISTORY AND FREQUENCY OF CLINICAL SCARLET FEVER CASES AND OF INJECTIONS FOR ARTIFICIAL IMMUNIZATION AMONG NINE THOUSAND FAMILIES, BASED ON NATION WIDE PERIODIC CANVASSES, 1928-1931. S. D. COLLINS, Pub. Health Rep. **53**:409 (March 18) 1938.

For a twelve month period from 1928 to 1931, 8,758 white families in 130 localities in 18 states were studied. In this group, 4 per cent of the 10 and 11 year old children and 3 per cent of the 15 to 19 year old group were immunized against scarlet fever. Thirteen per cent of the children studied gave a history of scarlet fever. Of the total 230 cases of scarlet fever, 208 occurred in children under 15 years of age. Of these cases, 14.2 per thousand were in children who had never been immunized; 2.8 per thousand were in children who were reported as having been previously attacked, and 4.7 per thousand were among children who reported injections for immunization against scarlet fever.

SANFORD, Chicago.

POLIOMYELITIS—CLINICAL OBSERVATIONS AT MEMPHIS DURING 1936-1937. G. J. LEVY, South. M. J. **31**:71 (Jan.) 1938.

A series of 87 cases of poliomyelitis occurring at Memphis, Tenn., in 1936-1937 is reported. In 78 cases the onset was abrupt, with fever, headache and vomiting. Sixty-four patients (73.6 per cent) showed evidence of paralysis during their stay in the hospital. Convalescent serum administered either in the pre-paralytic or in the paralytic stage had no appreciable effect on the outcome.

The fatality rate was 12.9 per cent in 1936 and 33.3 per cent in 1937. The combined mortality for 87 cases was 20.6 per cent. The mortality of the Negro patients (1 death) was 5.5 per cent.

SCHLUTZ, Chicago.

THE INTRADERMAL TEST IN WHOOPING COUGH: A REVIEW, WITH A STUDY OF THIRTEEN HUNDRED CASES. A. R. THOMPSON, J. Hyg. **38**:104 (Jan.) 1938.

A summary of the literature (here reviewed) on the value of the intradermal test in diagnosing whooping cough shows conflicting views.

In experiments with preparations for use in skin tests it was found that this confusion is largely explained by the type of test material used. Sauer's vaccine used as a test material gives a nonspecific reaction rather than an allergic reaction of specific value, and the result cannot be correlated with the clinical history. The intradermal response to pertussis endotoxin (prepared with extracts from mechanically disrupted bacilli after the method of Krueger) was much better. Positive reactions occurred in 85 per cent of children with a past history of whooping cough. Similar reactions elicited in 30 per cent of children who had no history of the disease are explained on the basis that these children had had subclinical pertussis and therefore their allergic response.

As judged by the test with pertussis endotoxin, bacterial hypersensitiveness appears about the tenth day of whooping cough and becomes more marked as the infection progresses. "Ultimately this cutaneous allergy shows regression which, however, is not always complete."

The pertussis endotoxin test is believed to be of some value in assessing immunity and in diagnosing whooping cough in an atypical or early form when the cough plate has been disappointing. Directions for the preparation of the test materials and for reading and tabulating the results of tests are given in detail.

JANNEY, Wauwatosa, Wis.

CERTAIN MODERN AGENTS FOR THE DETECTION AND ABOLITION OF SUSCEPTIBILITY TO DIPHTHERIA. C. W. ADEY, M. J. Australia **1**:47 (Jan. 8) 1938.

Based on a review of the recent literature, Adey concludes that (1) the most suitable prophylactic agent for immunization against diphtheria is ordinary toxoid (anatoxin), (2) a single dose of alum-precipitated toxoid may leave a large proportion of recipients still susceptible to the disease and, moreover, may occasionally cause severe local and general reactions, even small sterile abscesses and (3) insufficient evidence has accumulated to determine whether alum-precipitated toxoid administered in two doses is fully effective and whether it is innocuous.

GONCE, Madison, Wis.

TYPES OF CORYNEBACTERIUM DIPHTHERIAE PREVALENT IN VICTORIA AND THEIR CLINICAL SIGNIFICANCE. T. S. GREGORY, M. J. Australia **1**:57 (Jan. 8) 1938.

Investigations carried out in the state of Victoria emphasize the fact that the distribution of the types of diphtheria bacilli (mitis, gravis and "intermediate") found on culture of material obtained from apparently healthy children tends to vary from district to district and that cultures from children with diphtheria tend to be chiefly of the gravis or of the "intermediate" type in any one area. In view of these facts it seems that the severity of outbreaks of diphtheria and the death rate from the disease will vary according to the type of bacillus introduced into a population where only a small proportion of children have become naturally or artificially immunized. If a gravis strain is so introduced, many cases may quickly occur in which toxic complications are common and antitoxin fails to save life, especially if there is the slightest delay in treatment. The only method of avoiding the serious consequences of malignant diphtheria, of which the gravis type is the most frequent cause and which seems to be on the increase, is widespread prophylactic immunization of susceptible children.

GONCE, Madison, Wis.

IMMUNITY STUDIES IN DIPHTHERIA. H. L. CARRUTHERS, M. J. Australia **1**:59 (Jan. 8) 1938.

One hundred and five children whose reaction to the Schick test was positive were divided into two groups: those having a positive skin (Maloney) reaction to diluted formaldehydized diphtheritic anatoxin constituted group A, and those having a negative reaction, group B. The children in group A were given anatoxin at three weekly intervals in doses of 0.5, 0.75 and 1 cc.; those in group B were treated similarly except that the dose was much smaller, depending on the severity of the Maloney reaction. A Schick test was applied in both groups three weeks after each injection. In group A 27.1 per cent became negative to the test after the first injection and 64.45 per cent after the second. In group B 43.3 per cent became negative after the first injection and 34.78 per cent after the second. The results in group A provide evidence, first, of a satisfactory response of the antibody-producing mechanism to an initial extraneous stimulus and, second, of a prompt and abundant rise in antitoxin after the second injection. The results in group B suggest a difference between the antibody response to anatoxin and the antibody response due to natural stimuli. It seems easier to immunize artificially subjects who respond to the Schick test but give no reaction to the skin test anatoxin. At any rate, antibody response, either primary or secondary, to natural or artificial stimuli is subject to considerable variation in nature and degree.

GONCE, Madison, Wis.

TREATMENT OF WHOOPING-COUGH. E. H. R. HARRIS, Practitioner **140**:277 (March) 1938.

Whooping cough is now the most serious of the acute specific diseases of childhood, the fatality rate exceeding that of measles.

There are few diseases for which remedies more numerous or diverse have been proposed. For some of these, extravagant claims are made after clinical trials which are manifestly inadequate or uncontrolled.

Whether for prophylaxis or treatment, the old type of vaccine, prepared from stock cultures, is admittedly valueless. During the last few years, as the result chiefly of the pioneer work of T. Madsen in Denmark (1933), P. H. Leslie and A. D. Gardner in England (1931) and L. Sauer in the United States (1935), considerable advances have been made.

Sauer, a chief advocate of vaccines for prophylaxis, has no opinion of their usefulness in treatment, and in general it may be observed that the more carefully the results are controlled the less impressive do they appear. The literature is extensive, international and contradictory, but the fact emerges that vaccines employed in the paroxysmal stage are useless. This statement applies not only to vaccines, simple or mixed, as ordinarily understood, but to the various preparations of endotoxin derived from the bacillus.

Apart from any potential specific effect, it is undoubted that an injection of from 40 to 50 cc. of parental whole blood will sometimes turn the scale in a desperate case of whooping cough (or measles) complicated by bronchopneumonia, probably by the provision of complement.

Of the numerous drugs recommended for the control of the paroxysms, three are outstanding, namely: belladonna, ephedrine and phenobarbital.

Of the major complications, the commonest and the chief causes of death are bronchopneumonia and convulsions. Convulsions are usually confined to infants. The child who is most liable to convulsions during an attack of whooping cough is one who is the actual or potential subject of tetany—the fat, flabby infant in whom other stigmas may be elicited.

GELSTON, San Francisco.

USE OF PLACENTAL GLOBULINS IN CERTAIN INFECTIONS OF CHILDHOOD. O. FELSENFELD, Arch. de méd. d. enf. **41**:30 (Jan.) 1938.

Secondary effects following the injection of animal serums obligate the clinician to employ human serum whenever possible. It is an established fact also that the use of convalescent serum gives excellent results, but frequently such therapy is not possible because such serum is not available. The introduction of placental serum therefore has met with a most favorable reception, particularly in the prophylaxis and treatment for measles. Substituting 4 cc. of the immune globulin for the 5 to 20 cc. of convalescent serum formerly used, the author has obtained a satisfactory response. The injections are followed by slight rises of tempreature but without symptoms of allergy. Of 209 children treated in the pavilion for patients with contagious diseases at the Regional Institute for Tuberculous Children in Kosumberk, Czechoslovakia, only 2 contracted measles and then in attenuated form.

For therapeutic use, from 5 to 10 cc. is injected, with uniform amelioration of all symptoms and freedom from the usual complications.

The value of placental globulins in the prevention of scarlatina has also been compared with that of antitoxin and that of convalescent serum. During the years of 1936 and 1937, 352 children were exposed to this contagion. Among these, 136 were each given 10 cc. of convalescent serum, and 4 of this group contracted scarlet fever; 25 received from 5 to 10 cc. each of antitoxin and in 2 of them scarlet fever developed, while among 191 given injections of 4 cc. of placental globulin only 2 became ill with scarlatina. The relative percentages were 2.9, 8 and 2. In all cases the infection was attenuated. In this disease, results similar to those found in measles were obtained when the globulins were used therapeutically. No effect was produced in invasions of rubeola, but in 19 children exposed to mumps the epidemic was arrested through the prompt use of this agent.

AMESSE, Denver.

DIPHTHERITIC PARALYSES. J. JOSÉ, Arch. de méd. d. enf. **41**:129 (March) 1938.

Writing from the national center for control of diphtheria at Montevideo, Uruguay, José introduces his extensive monograph with the statement that all of the acute contagious infections of childhood, regardless of their causes, may be concerned with profound nervous sequelae. Diphtheria of the grave type is prone to manifestations of such an elective tropism, generally assembled under the designation of diphtheritic paralyses. A complete history of this syndrome is included, beginning with its first description, by Maingault in 1854. A thorough amplification on the progress of such paralyses is concluded by the following résumé: 1. Diphtheritic paralysis is less frequent in children than in adults. 2. These paralyses are directly due to the toxin. Clinically, they invariably begin with involvement of the soft palate. 3. It is essentially a paralysis of tonus. 4. The evolution and the prognosis depend more on the toxic and polyvisceral picture than on the extension of the process. 5. The treatment should not be confined to serotherapy but should include so-called shock treatment, i. e., the use of antityphoid or antigonococcic vaccines, which are often surprisingly efficient although their action cannot be satisfactorily explained from an immunologic point of view.

AMESSE, Denver.

ORCHITIS FOLLOWING VACCINATION AGAINST SMALLPOX. I. H. ALANTAR, Monatschr. f. Kinderh. **72**:390 (March) 1938.

Orchitis developed five days after vaccination against smallpox. The condition lasted three days, ending in perfect recovery.

GERSTLEY, Chicago.

THEORY AND PRACTICE IN THE TREATMENT OF POLIOMYELITIS. O. KAUDERS, Wien. klin. Wchnschr. **51**:17 (Jan. 7) 1938.

"What about intralumbar vs. intramuscular injections of reconvalescent serum in treating poliomyelitis?" asks Kauders. He notes that certain objections have been raised against the intralumbar method because the phenol usually added to the serum in the concentration of 0.5 per cent may adversely affect the leptomeninges. Certainly these membranes constitute an important barrier which must be broken through before the virus can enter the central nervous system. This fact argues against the theory that the virus enters the body along the nerve channels exclusively, and it is therefore a point in favor of treatment by other than the intramuscular method.

Other arguments in the case for intralumbar injections are based on four findings: 1. The cerebrospinal liquor shows definite changes even before the appearance of symptoms of paralysis. 2. These changes can be demonstrated as long as ten weeks after the acute stage of the illness. 3. The hemolysin reaction is positive in many cases, indicating that the permeability of the blood-liquor barrier has been disturbed. 4. The matter of the occurrence of abortive, and especially of meningeal, symptoms cannot be explained by the theory that the spread of the virus is by way of the nerves but is clarified by the assumption that the infection of the nerve parenchyma precedes the involvement of the entire organism and particularly that of the leptomeninges.

In Kauder's experience intralumbar injection of the serum has never caused the least unfavorable reaction even in cases in which paralysis had already developed. He recommends the method unreservedly. He uses 10 cc. (slightly less for small children) and occasionally repeats the dose, although usually the follow-up injection is intramuscular. He believes that the probability of a favorable effect against the onset of paralysis is greater if the intralumbar method is adopted.

He also believes an active course of therapy should be instituted following the acute stage of the disease. To what extent the lost function may be restored is problematic, but he is opposed in any event to the theory of *laissez faire* which is

favored in some quarters. Prognosis offers three possibilities: 1. The fall in ganglion cell elements of the anterior horn of the spinal cord can be compensated for in large measure through assumption of function by the uninjured ganglion cells. 2. The injured ganglion cells may be regenerated; the course of the disease is reversible, and function may be restored. 3. Apart from the basic organic process, a "training" of the disturbed function may be brought about, which is nothing but bringing the influence of the periphery to bear on the central nervous system. The latter fact is the reason for all exercise and motion therapy. Such exercise is also believed to be favorable to the "compensation" process affecting the uninjured ganglion cells. "Reversal," however, may be considerably delayed even in the most promising cases, since it is well established that histologic changes in poliomyelitis may last long beyond the acute stage.

Kauders believes that malaria treatment in the postacute stage is beneficial. Theoretically the malaria counteracts fever and infiltration. It has proved especially successful as a means of starting a swing back to normal after weeks of other therapeutic measures had failed to show results. Often dramatic recovery of muscle function has followed the use of the malaria treatment, though there may be a lapse of several weeks between the treatment and any noticeable improvement. Recovery of the locomotor function of the legs seems to be a specific result in many cases.

After malaria treatment, excellent results have tended to follow underwater exercises, massage and the other usual methods of muscle restoration (and eventually diathermy), even in cases in which before the use of malaria such methods were unsuccessful. Good results have also been reported through the use of faradic rays. All therapy should be carried on unremittingly for many months in an effort to prevent atrophy and contracture. Consultation with the orthopedist in this regard is recommended.

ABT, Chicago.

Acute Infectious Diseases

FEVER THERAPY IN THE TREATMENT OF ACUTE RHEUMATIC FEVER. F. L. DUNN and E. E. SIMMONS, Ann. Int. Med. **11**:1600 (March) 1938.

Fifteen patients with rheumatic fever were treated by means of the Kettering hypertherm. Three of the patients were children. The results indicated that the treatment produced symptomatic relief but that its effects on the subclinical manifestations of acute rheumatic fever were uncertain and that final evaluation must await further studies.

READING, Galveston, Texas.

EXANTHEM SUBITUM: REPORT OF A CASE. M. CUTTS, Ann. Int. Med. **11**:1752 (March) 1938.

The patient was a woman aged 31 years. The course of the disease, physical findings, laboratory data and other details were identical with the findings of exanthem subitum as encountered in infants and children. Cutts could find no previous record of a case occurring in an adult.

READING, Galveston, Texas.

MODE OF ACTION OF ZINC SULFATE SPRAY IN PREVENTING INFECTION WITH NASALLY INSTILLED POLIOMYELITIS VIRUS. A. B. SABIN and P. K. OLITSKY, J. Bact. **35**:44 (Jan.) 1938.

Sabin and Olitsky used a virus so potent that all untreated monkeys receiving it intranasally became paralyzed. Only zinc sulfate, of many chemicals tested so far, induced resistance with regularity. Among monkeys sprayed daily for seven days, 95 per cent (18 of 19) resisted virus given two days after the last spraying, 90 per cent (9 of 10) at one month, 57 per cent (8 of 14) at two months and none of 4 at three months. One thorough spraying on each of two days, also

a single spray, proved equally effective against virus given two days and one month later. The majority of monkeys (8 of 10) resisted infection when sprayed two hours after being given virus, but only 1 of 4 at six hours.

Mixture of virus with 1 and 4 per cent zinc sulfate incubated in vitro and then instilled intranasally induced paralysis in each of 4 monkeys. No definite correlation was found between acidity, protein-precipitating capacity or the ratio of protein to chemical at which precipitates completely redissolve and the capacity of different chemicals to protect monkeys for prolonged periods. Zinc sulfate is least acid, with a p_H of 5.2, and other chemicals with even more capacity for precipitating protein exert little or no protective action. The matter of whether or not the effectiveness of zinc sulfate is due to formation of an intracellular zinc compound which is slowly dissociable, the resistant state disappearing when the dissociation reaches a certain level, is now being investigated by the authors.

STOESSER, Minneapolis.

OVER-STIMULATION OF THE VAGUS NERVE IN RHEUMATIC FEVER. J. D. KEITH, Quart. J. Med. **7**:29 (Jan.) 1938.

Keith studied the PR interval by taking electrocardiograms of a series of rheumatic children. He was able to confirm the observation that a prolonged PR interval is one of the most characteristic abnormalities in the electrocardiograms of patients suffering from rheumatic fever.

In a series of 26 normal children the average PR interval was 0.138 second.

In a series of 200 children with rheumatic fever and chorea, 80 per cent of a group of 86 children with carditis showed PR intervals increased more than 0.2 second, and 81 per cent of a group of 59 children with chorea and carditis, 50 per cent of a group of 43 children with chorea without carditis and 58 per cent of a group of 12 children with arthritis without carditis showed similar changes in the auriculoventricular conduction time.

After the administration of atropine to a series of 11 children with rheumatic carditis there was an average reduction in the conduction time of 0.048 second. In a control series of normal children atropine produced an average reduction of the PR interval of 0.013 second. Epinephrine produced an average decrease of 0.027 second.

Keith discusses various theories which might explain prolongation of the conduction time in rheumatic fever and presents evidence to suggest that overstimulation of the vagus as a result of direct overactivity of the parasympathetic nerve endings in the heart may be the correct mechanism. The relation of overstimulation of the vagus to the bradycardia sometimes observed in rheumatic patients and to abnormal pain and vomiting is also discussed.

BRADFORD, Rochester, N. Y.

THE DOG TICK HAEMAPHYSALIS LEACHI AS A VECTOR OF TICK TYPHUS. J. H. S. GEAR and M. DOUTHWAITE, South African M. J. **12**:53 (Jan. 22) 1938.

Laboratory experiments of the authors incriminate the dog tick Haemaphysalis leachi as a vector of tick typhus in South Africa.

GONCE, Madison, Wis.

A CASE OF TYPHUS FEVER CONTRACTED IN THE LABORATORY FROM A VIRUS ISOLATED FROM RATS. J. H. S. GEAR and L. H. BECKER, South African M. J. **12**:57 (Jan. 22) 1938.

Gear and Becker report typhus fever in a laboratory worker caused by a virus isolated from the brains of wild rats. The features distinguishing this variety of typhus from the tick typhus occurring in South Africa are discussed.

GONCE, Madison, Wis.

CAN MALARIA CAUSE PERIPHERAL NERVE PALSY? M. N. DE and S. C. SEAL, Indian J. Pediat. **5**:8 (Jan.) 1938.

De and Seal report a case of malignant tertian malarial infection in a 2 year old child in whom the right facial nerve was involved along with the general nervous system.

GONCE, Madison, Wis.

SPOROTRICHOSIS IN CHILDREN. W. SCHULTZ RIBEIRO, Arch. de pediat., Rio de Janeiro **10**:283 (March) 1938.

The author classifies cases of sporotrichosis into two main groups: The first is comprised of cases in which Sporotrichum schenckii, Sporotrichum beurmanni (vareity asteroid and vareity indicum) and lastly Sporotrichum Jeanselmei are found to be the causal agents. The second group comprises cases in which Sporotrichum gougeroti is found. Common to all these cases are the symptoms of an initial lesion, dermatitis and adenopathy. The diagnosis is made on isolation of the organism. The author uses sulfanilamide by intramuscular injection, 5 cc. a day, for fourteen injections on alternate days.

SANFORD, Chicago.

PERMANENT MYOCARDIAL DAMAGE AFTER INFECTIONS. S. EDERER and I. VON ZARDAY, Monatschr. f. Kinderh. **72**:351 (March) 1938.

In an effort to determine the effect of various general infections on the myocardium, Ederer and von Zarday studied 91 children. The group consisted of 53 boys and 25 girls, the majority of whom were aged between 8 and 12 years. Forty-seven suffered from tonsillitis, diphtheria, rheumatic fever and grip; the remainder were infected with all the usual diseases of childhood. Besides clinical examinations, the study included roentgenographic and electrocardiographic studies.

Half of the group disclosed systolic murmurs, tachycardia or some muffling of the heart tones. One third of them (23) showed some cardiac change in the roentgenogram, and the electrocardiogram revealed abnormalities of the ST wave. There were also instances of low voltage, sinoauricular block, extrasystoles and in 14 patients changes of the T wave.

It is interesting to note that the children who acquire cardiac disturbances belong to the asthenic group.

GERSTLEY, Chicago.

Chronic Infectious Diseases

EFFECT OF CONTAGIOUS DISEASES ON PULMONARY TUBERCULOSIS AND ON THE TUBERCULIN REACTION IN CHILDHOOD. J. P. NALBANT, Am. Rev. Tuberc. **36**:773 (Dec.) 1937.

A total of 147 cases of acute infectious diseases in a group of children convalescing from pulmonary tuberculosis of the childhood type were carefully observed for any possible effect that an intercurrent infection might have on the primary disease. Of these children, 43 had measles; 39, chickenpox; 16, whooping cough; 13, scarlet fever; 30, mumps, and 6, diphtheria. No definite evidence was found to support the prevalent belief that any of these diseases has a deleterious effect on tuberculous lesions in the lungs of children.

A study of the effect of these diseases on tuberculin sensitivity also failed to show any definite depression of allergy to tuberculin in children with healed or active tuberculosis. The Mantoux method was used in all cases, and since most previous observers have used the Pirquet method of testing, this may explain the discrepancy in their findings.

EUGENE H. SMITH, Ogden, Utah.

STREPTOCOCCUS THROAT INFECTIONS IN TUBERCULOUS CHILDREN. G. F. MITCHELL, Am. Rev. Tuberc. **36**:778 (Dec.) 1937.

An epidemic of sore throat occurred in the childrens' division of a sanatorium, affecting 73 per cent of the 121 children, nearly all of whom had the childhood type of tuberculosis; 21 children had two attacks of sore throat and 4 had three attacks. An unusually high incidence of otitis media was observed and a greater incidence of pneumonia than is usually found in nontuberculous children. The number of children showing roentgenographic evidence of increase in their tuberculous infection was found to be definitely greater than is usually observed in the course of routine check-ups.

EUGENE H. SMITH, Ogden, Utah.

ROENTGENOGRAPHIC FEATURES OF TUBERCULOSIS IN BONES AND JOINTS. C. G. SUTHERLAND and E. A. ADDINGTON, Am. Rev. Tuberc. **37**:31 (Jan.) 1938.

Tuberculosis of bone is usually secondary to a primary infection in the lungs. In most of the cases this first focus of infection has healed, but occasionally the disease has proceeded to the secondary stage (adult pulmonary tuberculosis). In rare instances the port of entry may be the intestine, the skin, the tonsil or a wound, as in a case of ritual circumcision. From an infected focus an embolus of bacilli may reach the blood stream directly or by way of the thoracic duct. Lodgment in the osseous system usually occurs at a point between two sources of blood supply, where there is a slowing of the current favoring localization of the infectious organisms. Lymphoid tissues are the great feeding grounds for tubercle bacilli, and favorable conditions are present also in the spongy ends of long bones, where the marrow is of the lymphoid variety.

The outstanding roentgenographic characteristic of osseous tuberculosis is a translucency of the bone shadow without evidence of proliferation. Tubercles in the marrow or haversian canals act as foreign bodies and provoke hyperemia with resulting decalcification. As hyperemia subsides, the excess of calcium is again utilized so that there is an alternative decalcification and recalcification, varying with the degree of hyperemia. Sequestration is rare in tuberculous disease of bone because of the peripheral and periosteal hyperemia which the tubercle excites; hyperemia is essentially a decalcifying agent. Serous subperiosteal effusion takes places especially at the middle segment of a bone, with later formation of new bone, giving rise to the characteristic fusiform shape. The new bone is nodular and porous and forms a cylindric sheath about the original body of bone in which decalcification is proceeding. Destruction of the overlying cartilages may also occur, but the process takes place more slowly than with bone. As the hyperemia about the joint diminishes, local accumulations of calcium are utilized, the surface becomes nodular, ankylosis takes place and the tuberculous arthritis undergoes "spontaneous cure."

"In general, rarefaction with little or no reaction of tissues and a clouding of any joint due to effusion should at least arouse a suspicion of tuberculosis as the etiological factor."

EUGENE H. SMITH, Ogden, Utah.

EFFECT OF VITAMIN C ON THE CULTURE OF H_{37} TUBERCLE BACILLUS. F. H. HEISE and W. STEENKEN JR., Ann. Int. Med. **11**:1039 (Dec.) 1937.

This article can be abstracted best by giving in substance the authors' summary: Ascorbic acid added to the Proskauer-Beck synthetic medium alters the character of the growth of tubercle bacilli floated on it. On this medium Rv variants of the H_{37} strain develop like Ra variants whereas in control broth, without ascorbic acid, the growth retains the Rv characteristics. There is no associated alteration in the virulence of the organisms.

READING, Galveston, Texas.

RESIDUAL LESIONS IN HEALED TUBERCULOUS MENINGITIS. C. B. COURVILLE and H. S. EVANS, Bull. Los Angeles Neurol. Soc. **2**:125 (Sept.) 1937.

Many cases of healed tuberculous meningitis have been reported, especially as regards the older age periods. In only 2.5 per cent of the cases previously reported were the patients less than 2½ years of age, while in 30 per cent they were over 20. Courville and Evans report 3 cases in children in which healed tuberculous lesions were demonstrated in the meninges after death. In case 1, that of a Mexican girl aged 7 years, with no history of previous illness, the clinical diagnosis was verified by inoculation of guinea pigs. She died fifteen days after admission to the hospital, and necropsy revealed solitary and conglomerate calcareous tubercles scattered over the dorsolateral surfaces of the cerebral hemispheres. There were also clusters of tubercles in the right lung and adhesions in the right pleural cavity. In case 2 a Mexican boy aged 3 years was found to have tuberculous meningitis and was returned to his home with the prognosis of a probable fatal outcome, although the organism was not discovered in the cerebrospinal fluid. A year later the child had what was thought to be infantile paralysis; later, tuberculous osteomyelitis appeared in both feet and was followed by tuberculosis of the ribs and sacroiliac joints. The boy died of pulmonary tuberculosis eight years after onset of the illness. Autopsy revealed adhesions about the medulla oblongata, with advanced hydrocephalus, but no tubercles in the leptomeninges. A calcified tuberculoma was observed in the white matter beneath the right cingulate gyrus, and a noncalcified tuberculoma was discovered in the left cerebellar hemisphere. In case 3 a Mexican boy aged 6, with no history of previous illness, presented evidences typical of tuberculous meningitis, a lowered sugar content of the cerebrospinal fluid and increased density of the left hilus in roentgenograms of the chest. Death occurred four weeks after onset of the illness. At autopsy a few miliary nodules were seen in the meninges of the brain, some of which were healed and calcified and contained new formed bone. A noncalcified small tuberculoma was present in the genu of the corpus callosum.

Courville and Evans conclude that healing in tuberculous meningitis depends not only on local tissue resistance but on minimal meningeal infection. These cases lend support to the belief that many of the cases in which healing was reported were true instances of tuberculous meningitis, even though the bacillus was not demonstrated during the acute stage.

MACKAY, Chicago. [ARCH. NEUROL. & PSYCHIAT.]

FURTHER STUDIES WITH THE TUBERCULIN OINTMENT PATCH TEST. E. WOLFF and S. HURWITZ, J. A. M. A. **109**:2042 (Dec. 18) 1937.

The preparation of a tuberculin ointment and a control ointment for a patch test and the technic of application are given. In more than 1,000 cases in which this test and the Mantoux test were compared, there was 98.2 per cent agreement. The discrepancies occurred only in patients whose disease was clinically latent.

HEERSMA, Kalamazoo, Mich.

A COMPARATIVE STUDY OF THE LEVINSON AND TRYPTOPHAN TESTS AS AIDS IN THE DIAGNOSIS OF TUBERCULOUS MENINGITIS. F. X. GIUSTRA, J. Pediat. **11**:805 (Dec.) 1937.

The Levinson and tryptophan tests were done on the spinal fluids of 35 patients who had some involvement of the central nervous system. Ten of the patients were proved to have tuberculous meningitis. The Levinson test was positive for all those with tuberculous meningitis whereas the tryptophan test was positive for only 30 per cent of these. Of those with nontuberculous involvement, the Levinson test was positive for 16 per cent and the tryptophan test for 8 per cent; the 2 patients for whom the tryptophan test was positive presented purulent spinal fluid. Giustra concludes that neither test should be considered an important aid to the present routine methods of making or excluding a diagnosis of tuberculous meningitis.

RAUH, Cincinnati.

TREATMENT OF PRENATAL OR CONGENITAL SYPHILIS. H. R. FOERSTER, Wisconsin M. J. **36**:987 (Dec.) 1937.

The term "prenatal syphilis" has been nationally accepted to replace that of hereditary syphilis, which is wholly incorrect. Syphilis cannot be transmitted by the germ plasm and therefore cannot be inherited. Early infection of the fetus results in abortion or miscarriage. In most stillborn infants and in infants born with active syphilis the disease has its inception after the fifth month of intrauterine life. From 8 to 10 per cent of the women attending prenatal clinics have positive serologic tests, and about 2 per cent of the total number of children born in the United States have prenatal syphilis.

Among 268 patients with prenatal syphilis who came to a clinic, only 32 per cent came because of symptoms resulting from syphilis, which indicates the need for routine serologic tests, especially in pediatric clinics. Only 18 per cent came under treatment during the first three years of life; 38 per cent were over 15 years of age, the most effective period for treatment having been passed.

Symptoms of syphilis were present in 111 patients; 44 per cent had ocular lesions, 6 per cent cutaneous, 6 per cent auditory, 15 per cent neurologic and 11 per cent bone lesions. Fifty patients exhibited stigmas of prenatal syphilis (84 per cent dental).

The serologic tests on 167 patients on admission were strongly positive; the tests on 23 were negative. Six patients had negative serologic tests throughout treatment and in the presence of active lesions, and the serologic tests of several others relapsed to positive during the treatment. On termination of treatment 80 per cent gave negative results. Among those still giving positive reactions were patients with neurosyphilis.

No treatment may be considered complete until the findings in the cerebrospinal fluid are negative.

Among 1,000 serologic tests made there was an absolute disagreement between the Kline and Wassermann tests in 18 instances. The Kline test, more sensitive, remained strongly positive in some cases in which the patients had been inadequately treated when the Wassermann test had become negative.

Among 50 patients with syphilis who were pregnant were 21 with prenatal syphilis; 17 of these had been inadequately treated before pregnancy. Under adequate treatment of 34 of these patients 33 apparently normal infants were delivered. The only death, that of a premature infant, was not due to syphilis. Among 24 patients inadequately treated during prgenancy there were 5 stillbirths and 1 premature birth.

The treatment of prenatal or congenital syphilis may be divided into three stages: 1. Preventive treatment. This is both preconceptional and postconceptional. Routine serologic tests should be done in public clinics and by obstetricians with a view to instituting preconceptional treatment when needed. With energetic treatment throughout pregnancy, the infant will be delivered symptom free in 90 per cent of the cases. On delivery serologic tests should be made on the cord blood and then on the infant at 8 weeks of age. "A syphilitic child may remain seronegative until as late as the 5th year."

2. Treatment of early prenatal syphilis. This comprises therapeutic measures used at any time from birth through the second year. It may start with mercury rubs and with administration of acetarsone or more energetically with intramuscular therapy. The response is in direct proportion to the age of starting and the amount of treatment. Bismuth salicylate, neoarsphenamine (intramuscularly) and bismarsen are favored. A total of twenty-four injections of an arsenical or of thirty or more of an insoluble preparation of bismuth or mercury should be given over a period of from two to three years.

3. Treatment of late prenatal syphilis. This is much like that of late syphilis in the adult. Thorough and prolonged treatment is needed, with frequent general examinations (blood urine spinal fluid, etc.). Fever therapy may be combined with routine chemotherapy and should extend over at least three years.

JANNEY, Wauwatosa, Wis.

TREATMENT OF TUBERCULOSIS BY NEEDLE PUNCTURE OF THE LUNG. C. R. LAVELLE, Lancet **2**:1299 (Dec. 4) 1937.

In stereoscopic roentgenograms of patients with pulmonary tuberculosis Lavelle observed a lesion in the lung similar to the tuberculous nucleus or focus found in bone. With the puncture of this nucleus in the lung he claims to have obtained to an even greater degree the beneficial results—both local and systemic—that he described following the perforation of the tuberculous focus in bone—i. e., speedy detoxication, increased appetite and weight, good color, increased tension of pulse and other gains. He claims beneficial results in from 76 to 80 per cent of about 200 cases of tuberculosis of the lungs.

As the focus is generally placed under the pleura, the penetration of the needle is only to the extent of an inch or two. The curative effect of the puncture is explained on the basis that specific antibodies bound up in the nucleus are released into the blood stream by the puncture and then affect all the tuberculous lesions throughout the body.

LANGMANN, New York.

TREATMENT OF INTERSTITIAL KERATITIS COMPLICATING CONGENITAL SYPHILIS. E. LESNÉ and D. RONGET, Arch. de méd. d. enf. **41**:11 (Jan.) 1938.

It is asserted that in the majority of cases of interstitial keratitis properly directed therapy will result in complete and permanent cure, although relief may be considerably delayed. Interstitial keratitis appears most frequently in late childhood and is exceptionally seen in young adults; it is commonly the first manifestation of unsuspected syphilis, unilateral at onset and usually proceeding to bilateral involvement. Together with hydrarthrosis, simple or double, of the knee, it constitutes the well known syndrome of delayed congenital syphilis.

In the authors' series of 15 cases, mercuric cyanide was employed intravenously with satisfactory results; 10 patients recovered promptly without sequelae; 3 relapsed and were treated with a preparation of bismuth, while in 2 slight opacities persisted.

AMESSE, Denver.

MENINGITIS IN THE COURSE OF TUBERCULOUS INFECTION. P. NOBÉCOURT and S. B. BRISKAS, Arch. de méd. d. enf. **41**:17 (Jan.) 1938.

In estimating the period of onset of this meningeal complication in tuberculosis affecting subjects ranging in age from birth to 15 years, the authors utilize observations on 368 of 14,976 children hospitalized for tuberculosis between 1921 and 1937. The tables show an incidence of tuberculous meningitis of 2.4 per cent, with maximal frequency during the months of April, July, August and September.

It is admitted that the exact time of meningeal invasion is difficult to determine, especially in older children. In 2 instances a relative approximation could be made between the first positive skin reaction and the advent of meningitis. Of the series of 368 children who presented the complication, 120 were made the subject of intensive study, and 58 were carefully examined post mortem. The latter were classified into three groups: 45 showed recent foci of gangliopulmonary tuberculosis or generalized involvement; 10 showed caseous pulmonary foci, and 3 exhibited old lesions, including, in a child of 3 years, a cold abscess. Neither postmortem nor roentgenologic observations, however, permitted an opinion concerning the precise period of extension to the meninges. In determining the interval between contact and meningitis among 27 infants ranging in age from 2 to 10 months it was found that the time varied from 4 weeks to 3 months in 20 of these and from 4 to 6 months in 7.

Wallgren and Nelson asserted that the appearance of erythema nodosum signalizes the debut of tuberculous meningitis, but in the present series it preceded this disease in only a single case.

AMESSE, Denver.

COMPLEMENT DEVIATION WITH PETRAGNANI'S ANATUBERCULIN IN CHILDREN OF TUBERCULOUS PARENTS. F. TORELLI, Méd. inf. **9**:5 (Jan.) 1938.

Petragnani's anatuberculin was used as antigen in testing the serum of 145 subjects for complement deviation. Negative results were obtained with 30 healthy children. Positive reactions were obtained with 10 of 23 children who had latent tuberculosis and positive reactions to tuberculin. Of 31 children with active tuberculosis, 19 had positive reactions to the anatuberculin. The test seems to have little value in diagnosis; it is of some prognostic significance in that tuberculous patients in good physical condition were the ones to have positive reactions.

Tests were made on serum from each of 15 newborn infants of tuberculous mothers; blood was withdrawn from the umbilical cord at birth and from the baby on the first, fifteenth, thirtieth and sixtieth days of life. The serums of 6 of the infants gave negative reactions in all tests. The serums of the other 9 infants gave results as follows: The umbilical cord serums all reacted positively. Of serums tested twenty-four hours after birth, 7 retained the capacity to react positively. Of those tested at the fifteenth day of life, 5 still showed a positive reaction. Of those tested at the end of the first month, 4, and of those tested at the end of the second month, none, gave a positive reaction. In each instance when once a negative reaction was obtained the serum continued to give negative reactions. It is apparent that tuberculous antibodies pass from the mother to the fetus through the placenta and that these antibodies may persist for a period of less than two months.

HIGGINS, Boston.

TUBERCULOSIS OF INFANTS AND THE ULTRAVIRUS OF THE TUBERCLE BACILLUS. A. DUFOURT, Paris méd. **1**:17 (Jan. 1) 1938.

Dufourt is convinced of the presence of an ultravirus in tuberculous persons but does not consider it pathogenic in the ordinary sense. However, it can pass the placental barrier, and infants born of tuberculous mothers may show a syndrome of malnutrition in the first months of life thought to be dependent on this transmission. However, the ultravirus disappears rapidly from the organism and does not "mutate" into the virulent organism.

LESLIE, Evanston, Ill.

SYPHILIS TRANSMITTED TO AN INFANT BY INJECTIONS OF BLOOD. N. CARRARA, Lattante **8**:646 (Dec.) 1937.

An infant of 5 months presented a pyogenic infection of the skin. As treatment, several subcutaneous injections of from 2 to 10 cc. of whole blood were given, and the cutaneous infection promptly got better. Eleven days after the first injection the child began to show snuffles, fever and an enlarged spleen. These signs were believed to be the result of a grippal respiratory infection; but three days later the donor of the blood reported an eruption of the skin which was recognized as secondary syphilis. The donor's Wassermann reaction was found to be positive. On the death of the baby's mother, three months previously, the baby's Wassermann reaction had been negative. The Wassermann test was negative sixteen days but positive thirty-two days after the first injection. The child was treated by neoarsphenamine and showed a rapid and satisfactory response to treatment.

HIGGINS, Boston.

EXTRAPULMONARY TUBERCULOSIS IN THE CHILD AND ITS RELATION TO PULMONARY TUBERCULOSIS. G. SANPAOLESI, Riv. di clin. pediat. **36**:45 (Jan.) 1938.

Of 120 children with tuberculosis of the bones and joints or with other scrofulous manifestations, over 90 per cent had roentgenologic evidence of hilar lesions. Many showed parenchymal lesions of the lungs. Sanpaolesi feels that medical supervision is indispensable in the care of children with extrapulmonary tuberculosis.

HIGGINS, Boston.

ROENTGENOLOGIC STUDIES OF THE PRIMARY LESION OF TUBERCULOSIS. M. Y F. ARCE and P. CAMPUZANA, Arch. de med. inf. **6**:365 (Oct.-Dec.) 1937.

Twenty-one roentgenograms are shown, illustrating primary lesions of the lung. The authors rather favor the French and American classifications of Parrot and Ranke, and they quite agree with these concepts. They also advise the making of lateral as well as of anteroposterior roentgenograms.

SANFORD, Chicago.

PRIMARY TUBERCULOUS INFECTION OF INFANCY. C. PERNETTA, Arch. de pediat., Rio de Janeiro **10**:179 (Jan.) 1938.

A case of epituberculosis in the first year of life is discussed.

SANFORD, Chicago.

INCIDENCE OF TUBERCULOSIS IN CHILDHOOD. A. DIETRICH, Med. Klin. **33**:1637 (Dec. 3) 1937.

Dietrich found the incidence of tuberculous infection among Viennese children considerably lower than that found by Hamburger in 1909. He attributes the lower incidence (60 per cent by the fourteenth year) to preventive measures and proper treatment. Numerous figures on incidence, found in the literature, are discussed. For comparable studies, the social status of the subjects and the technic of tuberculin testing are important. Dietrich employed the Pirquet and Moro tests, and if these were negative he gave tuberculin (1:100, 1:10 or 1 mg.) subcutaneously.

SIEMSEN, Chicago.

EXTREME SECONDARY ANEMIA DUE TO CONGENITAL SYPHILIS. H. ZWAN-GOLDSCHIEDOWA, Pedjatrja polska **17**:112 (March-April) 1937.

This form of anemia is frequent in syphilitic children. However, the cases that attract attention are those in which the hemoglobin content falls to from 10 to 15 per cent. The patient whose case is reported here responded favorably after treatment with acetarsone (stovarsol) and preparations of iron.

KRUPINSKI, Chicago.

B. C. G. VACCINATION. J. H. RAYNAL, Chinese M. J. **52**:599 (Oct.) 1937.

Raynal, director of the French municipal laboratory at Shanghai, gives a short editorial on his experiences in the Far East. He concludes that BCG vaccination is efficacious in reducing both mortality and morbidity. It is a step forward in the war against tuberculosis, shown definitely in the protection afforded in the vulnerable years of early childhood.

NEFF, Kansas City, Mo.

JUVENILE DEMENTIA PARALYTICA. J. STRÖM, Acta psychiat. et neurol. **12**:355, 1937.

Ström reports 4 cases of juvenile dementia paralytica in girls whose mothers had syphilis. The disease was recognized in 3 of the patients at the beginning of the school age and in the fourth at the age of 11 years. The symptoms were progressive dementia, abnormal pupillary reflexes, mononucleosis and increased globulin content of the spinal fluid. In 2 patients there were trophic disturbances of the arm and leg. One patient was given malarial treatment, without success (the girl is now dead); the other 3, when treated with malaria, showed some

improvement in their mental deficiency. One of the girls is in such a state of health that there is reason to believe that she will be able to take care of herself in the future.

WALLGREN, Göteborg, Sweden.

ENDEMIC TUBERCULOSIS IN A PREPARATORY SCHOOL. A. SASSE, Nord. med. tidskr. **14**:1664 (Oct. 9) 1937.

Tuberculin tests on 15 children in a small preparatory school showed that all the children were tuberculous; 6 of the children had been found to give reactions to tuberculin from three to nine months previously. The source of their infection was a consumptive teacher, whose disease was diagnosed two months before the tuberculin tests were carried out. Three of the newly infected children had acquired erythema nodosum; others had displayed fever with catarrhal symptoms, and many of these had roentgenologic changes about the hilus. The latter were treated at a sanatorium for many months. The prognosis is good.

WALLGREN, Göteborg, Sweden.

Diseases of Blood, Heart and Blood Vessels and Spleen

PLASMA COLLOID OSMOTIC PRESSURE AS A FACTOR IN EDEMA FORMATION AND EDEMA ABSORPTION. A. C. KERKHOF, Ann. Int. Med. **11**:867 (Dec.) 1937.

In discussing the mechanism of edema Kerkhof points out the following factors that might be instrumental in causing an increase in transudation and thus lead to edema: (1) increased hydrostatic or capillary pressure, (2) decreased colloid osmotic pressure of the plasma, (3) increased permeability of the capillaries and (4) increased colloid osmotic pressure in the tissue surrounding the capillaries. Of these the first two are the most important.

The method of measuring the "oncotic" pressure as employed by Schade is recommended.

The normal colloid osmotic pressure of the blood plasma in man is said to be approximately 21.4 ± 2.5 mm. of mercury whereas in nephrosis and nephritis with edema the colloid osmotic pressure is usually lower than 15 mm. of mercury and averages 8 mm.

The injection of acacia increases the colloid osmotic pressure of the plasma and causes a disappearance of the edema, accompanied by diuresis of water and salt in the same proportions as they are found in the edema fluid.

READING, Galveston, Texas.

SPLENIC IRRADIATION IN THE TREATMENT OF PURPURA HAEMORRHAGICA. H. W. JONES, L. M. TOCANTINS and R. M. SMITH, Ann. Int. Med. **11**:1311 (Jan.) 1938.

Twelve cases of purpura haemorrhagica were studied. In 9 adequate treatment was given, but in 3 the amount of treatment was not sufficient to be conclusive. In none of the patients were the results favorable in comparison with reports of other observers.

In this condition roentgen therapy is not without danger. It may produce nausea and vomiting, with increased intracranial pressure and hemorrhage.

READING, Galveston, Texas.

TUBERCULOUS PERICARDITIS AND PICK'S DISEASE. G. F. MITCHELL, Arch. Pediat. **55**:157 (March) 1938.

Three cases in which many of the clinical features of Pick's syndrome were presented are reported. One patient died of the typical cardiac failure that characterizes death from Pick's disease. Two died of tuberculosis.

ORR, Buffalo, N. Y.

SEASONAL VARIATIONS IN CAPILLARY RESISTANCE OF INSTITUTION CHILDREN. LYDIA J. ROBERTS, RUTH BLAIR and MARIAN BAILEY, J. Pediat. **11**:626 (Nov.) 1937.

The capillary resistance of a group of children in an institution was determined by the Dalldorf resistometer at five different periods during the year. The results were studied in relation to the dietary supply of vitamin C, to the incidence of infection and to the amount of vitamin D available from sunshine at the different periods. The capillary resistance as thus determined revealed a distinct seasonal trend. The mean pressure for the group was low in February, dropped lower in April, rose somewhat in July, rose higher in August and dropped again to a lower level in November. The records of many individual children exhibited the same trend: Eighty-three per cent showed some tendency to follow the seasonal pattern; half of them revealed a decided correspondence, and 23 per cent revealed almost a perfect correspondence. No clearcut relation appeared between capillary resistance and the incidence of infection, but a striking parallelism was noted between the pressure found and the level of vitamin C in the diets. An almost equal correspondence was noted between resistance and the amount of vitamin D available from sunshine at the different periods.

The authors emphasize that in neither case can the parallelism be interpreted as necessarily indicating a causal relationship. They believe that the seasonal variation in resistance observed is too pronounced to be accidental.

RAUH, Cincinnati. [FROM THE AUTHORS' SUMMARY.]

CHRONIC NUTRITIONAL HYPOCHROMIC ANEMIA. L. S. P. DAVIDSON and H. W. FULLERTON, Edinburgh M. J. **45**:1 (Jan.) 1938.

This is an instalment of a contribution dealing with the causes and incidence of iron deficiency and with clinical manifestations of interest, especially with their frequency, cause and nature. The authors discuss chiefly this type of anemia in adults and especially the importance of achlorhydria as a causal factor. There is included a short consideration of the causation of iron deficiency in infants. It is not probable that there is a significant correlation between anemia of the infant and anemia of the mother. A study of iron metabolism in infants with a low level of hepatic iron at birth showed that this had little influence on the level of hemoglobin at a later time. But the smaller birth weights were found to correspond to low levels of hemoglobin at about the end of the first year.

Infective illness is an important factor in producing infantile anemia because of toxic inhibition of the formation of blood, increased excretion of iron during infection and reduction of iron intake during the feeding disturbances due to such illness. Achlorhydria occurs in infancy and may be responsible for diminished absorption of iron from the gastrointestinal tract. NEFF, Kansas City, Mo.

COOLEY'S ANEMIA (ERYTHROBLASTIC OR MEDITERRANEAN ANEMIA). M. MUKHERJI, Indian J. Pediat. **5**:1 (Jan.) 1938.

Mukherji reports a case of Cooley's erythroblastic anemia occurring in a 30 month old Hindu boy. The case is remarkable because (1) it establishes the possibility that the disease may be found in children of non-Mediterranean parentage and (2) it is the first recorded case east of Suez. GONCE, Madison, Wis.

RESULTS OF SPLENECTOMY IN A FAMILY WITH ACHOLURIC JAUNDICE. N. MAKAR, J. Egyptian M. A. **21**:13 (Jan.) 1938.

In 3 cases of familial congenital jaundice improvement followed splenectomy. In the mother, aged 34 years, the hemoglobin percentage improved from 50 to

80 in ten weeks, the jaundice disappeared, and the fragility of the red blood cells dropped from 0.54-0.44 to 0.5-0.38.

A daughter aged 10 years showed a similar response, with jaundice disappearing, the hemoglobin percentage improving from 65 to 85 in twelve weeks and the fragility of the red blood cells dropping from 0.58-0.41 to 0.5-0.38.

A daughter aged 6 years had no clinical jaundice, but a fragility test of the red blood cells gave 0.54-0.44, and the icterus index was 6 units before operation. In this child four weeks after operation the fragility of the red blood cells dropped to 0.5-0.34 and the hemoglobin percentage improved from 60 to 75. All these patients showed frequent epistaxis before operation and less frequent attacks afterward. No adequate explanation for this symptom was demonstrated.

MULHERIN, Augusta, Ga.

COPPER SULFATE IN THE THERAPY OF ANEMIAS OF ALL AGES. A. CANELLI, Rev. franç. de pédiat. **13**:494, 1937.

Canelli finds copper sulfate to be of value in the treatment of all types of anemia. He uses a 1 per cent solution and gives from 10 to 20 drops before the two principal meals for periods of ten days alternating with periods of cessation of this type of medication.

LESLIE, Evanston, Ill.

MODIFICATION IN THE SPEED OF THE SEDIMENTATION RATE OF THE BLOOD FROM MUSCULAR WORK. P. LUCIANI, Riv. di clin. pediat. **36**:15 (Jan.) 1938.

The sedimentation rate of the blood was observed in 36 children before and after they had run a distance of 300 meters in from two to three minutes. Following this exercise the sedimentation rate showed essentially no change in 12 healthy children, but was retarded in 22 of the 24 children who had subacute, nonfebrile illnesses or were convalescent from febrile illnesses. The sedimentation rate studied following exercise gives an index of fatigue in children.

HIGGINS, Boston.

MITRAL LESIONS. F. LAPORT, Arch. de pediat., Rio de Janeiro **10**:105 (Dec.) 1937.

This interesting article presents 15 cases of different mitral lesions, with roentgenograms and electrocardiograms. Measurements of the hearts are made from the roentgenograms, and their application is explained.

SANFORD, Chicago.

ERYTHROMELALGIA (WEIR MITCHELL DISEASE) IN A SYPHILITIC INFANT. F. HURTADO, T. VALLEDOR and C. HERNÁNDEZ MIYARES, J. pediát. de Santiago de Cuba, 1937, p. 137.

The child was 2 years old. The authors do not attribute the erythromelalgia to the child's syphilitic condition, but neither do they reject the possibility of syphilis having a share in its occurrence. They support the diagnosis with capillariscopic observations on the great toe of the left foot. An electrocardiogram revealed normotopic tachycardia without additional changes. Graphic records of arterial and capillary pressures, obtained by tonoscillograph, are submitted. After considering the Weir Mitchell syndrome from the standpoint of cause, pathogenesis and differentiation from such vascular syndromes as Raynaud's disease and acrodynia, the authors conclude that it should be classified among the functional disturbances of the sympathetic nervous system. Lastly, they refer to symptomatic treatment of their patient and to the specific treatment of the syphilitic infection which occurred concomitantly with it.

KALISKI, San Antonio, Texas.

SPORADIC HEMOPHILIA. J. C. SANTA MARIA and F. C. MILIA, Rev. Soc. de pediat. de Rosario **2**:151 (Sept.) 1937.

The authors conclude that the condition was due to a deficiency of vitamin C. Roentgenograms gave some slight evidence. Ascorbic acid was given, which caused a decrease in the coagulation time of the blood from sixty-five to thirty-five minutes.

SANFORD, Chicago.

A CASE OF LEUKEMIA LYMPHATICA ALEUKEMICA. K. ERECINSKI, Pedjatrja polska **17**:96 (March-April) 1937.

A 10 year old child, an orphan, came to the children's clinic because of pallor, anemia and enlargement of the glands in the axilla of three months' duration. The blood picture showed a reduction in the number of erythrocytes and disappearance of lymphocytes. Large doses of arsenic and vitamin C were given, but the child contracted acute sore throat and stomatitis and died. A postmortem examination demonstrated the aforenamed condition.

KRUPINSKI, Chicago.

ARTERIOSCLEROSIS IN AN EIGHT YEAR OLD BOY. E. THOMASEN, Ugesk. f. læger **99**:1290 (Dec. 2) 1937.

The boy since his third year had suffered from recurrent febrile articular symptoms without demonstrable bacteremia and without septic foci. When he was 8 years of age, a roentgenographic examination showed calcifications in the arteries of the arms and legs. These arteriosclerotic changes produced no clinical symptoms. The joints were found normal; the renal function, normal, and the calcium and phosphorus of the blood, normal. The author believes that the arteriosclerosis may be due to the fact that the boy when 4 years old periodically got vitamin D in insufficiently large doses.

WALLGREN, Göteborg, Sweden.

DETERMINATION OF THE MEAN DIAMETER OF ERYTHROCYTES AND ITS VALUE IN LIVER DISEASES AND ICTERUS. L. SCHALM, Nederl. tijdschr. v. geneesk. **81**:5786 (Dec. 4) 1937.

After comparing different apparatus for the determination of the mean diameter of erythrocytes, the author prefers the method of Pyper. It gave a mean diameter of 7.8 microns. In cases of serious damage to the liver tissue with jaundice, distinct macrocytosis (from 8.8 to 9.5 microns) was generally met with. In cases, however, of obstructive jaundice the mean diameter was not higher than 8.5 microns. In cases of jaundice caused by obstruction due to gallstones, this figure was never surpassed. The value of these findings for differential diagnosis if they should be confirmed by further observations on a larger scale is discussed.

VAN CREVELD, Amsterdam, Netherlands.

PERNICIOUS ANEMIA DURING PREGNANCY WITH DEVIATIONS IN THE BLOOD OF THE NEWBORN. S. VAN CREVELD and P. J. ZUIDEMA, Nederl. tijdschr. v. geneesk. **81**:5936 (Dec. 11) 1937.

The author describes a case of pernicious anemia of pregnancy, in which the condition was treated intensively but unsuccessfully with liver preparations. The prematurely born infant showed severe changes in the blood and in the hemopoietic organs (the liver and the spleen). The question is raised whether there exists a relation between the changes found in the infant and the treatment of the mother's anemia with liver preparations.

VAN CREVELD, Amsterdam, Netherlands.

CARDIOMEGALIA GLYCOGENICA CIRCUMSCRIPTA. S. VAN CREVELD and H. M. VAN DER LINDE, Nederl. tijdschr. v. geneesk. **81**:6000 (Dec. 18) 1937.

The authors present a description of a case of hypertrophy of the heart (resembling the pseudo-idiopathic type) with partial accumulation of glycogen in the

cardiac muscle. They add a discussion of the various possibilities which may explain this "cardiomegalia glycogenica circumscripta."

VAN CREVELD, Amsterdam, Netherlands.

Diseases of Lungs, Pleura and Mediastinum

SPONTANEOUS MEDIASTINAL AND SUBCUTANEOUS EMPHYSEMA IN CHILDREN. J. LEVEUF and R. KOHN, Arch. de méd. d. enf. **41**:156 (March) 1938.

This syndrome, although rare, has been recognized and discussed since it was first reported by Laënnec and has been described in detail by Dupuytren, Trousseau and numerous other writers. In reporting a case in a girl of 2½ years, Leveuf and Kohn call attention to certain diagnostic and therapeutic features. The child began to suffer from a catarrhal cold, with chills, moderate fever and a rasping cough. She was pale and extremely tired and voluntarily kept to her bed. Applications of mustard were violently resisted and were followed by severe attacks of vomiting. Breathing then became difficult, and medical aid was summoned.

Examination showed a child gravely ill; the face was ashen, the nostrils dilated, the eyes sunken and the lips of a violet hue; there was dyspnea, and the breathing was entirely abdominal. An area of edema could readily be made out in the presternal region, with crepitation and other signs of subcutaneous emphysema. Hot baths and sedatives were ordered at this stage. On the following day the emphysema involved the entire chest and neck. The menace from asphyxia was extreme, and the basic condition was considered to be mediastinal rather than subcutaneous.

The patient was operated on under ethyl chloride anesthesia. The incision was made at the base of the sternum, and the soft tissues were carefully separated by the finger. The entire picture was changed, and the little girl made a prompt and permanent recovery.

In a report of 10 observations by Comby, in 1914, there was mention of 4 fatalities. The urgency of the medical type of mediastinal emphysema usually prevents making roentgenographic studies, which could offer great assistance in diagnosis.

The mechanism of production and the differential diagnosis are considered at length.

AMESSE, Denver.

PULMONARY ABSCESS IN A CHILD OF THREE YEARS. C. HURMUZACHE, Bull. Soc. de pédiat. de Iasi **7**:85 (Oct.-Dec.) 1936.

The first symptoms produced by pulmonary abscess in the case reported were those of pseudomeningitis and pulmonary congestion. The diagnosis was made by roentgenogram and by aspiration of pus from the abscess, from which staphylococci and streptococci were cultured. An injection of 33 per cent alcohol was ineffective, and a pneumonotomy was performed. The outcome of the case remains uncertain.

LESLIE, Evanston, Ill.

BLOOD PHOSPHORUS IN PNEUMONIA. N. DUNKELMANN, Monatschr. f. Kinderh. **72**:364 (March) 1938.

Dunkelmann confirms previous observations that during the course of lobar pneumonia there is a diminution in blood phosphorus. The level returns to normal after recovery. He treated pneumonia with 30 drops of viosterol daily and thinks the results were satisfactory.

GERSTLEY, Chicago.

CYSTIC LUNGS. S. CHODKOWSKA, Pedjatrja polska **17**:90 (March-April) 1937.

This condition occurs rarely. Only 36 cases have been reported in the literature. Classification of this condition is impossible because the cause and pathogenesis

are not known. Some claim it is due to inflammatory processes. The cysts vary in size from that of a pinhead to that of a walnut. Some authors report that many varieties of tissue are found in these cysts.

KRUPINSKI, Chicago.

ABSCESSES OF THE LUNGS IN INFANTS. H. LASKIEWICZ, Pedjatrja polska **17**:101 (March-April) 1937.

Multiple abscesses of the lungs are rare. The chief cause is infection by way of the umbilicus. Abscesses due to pneumonia are frequent, however. Big solitary pulmonary abscesses are rare, particularly in infants. In thirteen years only 23 cases of abscesses of the lungs were found in 11,236 children, and of these only 6 were in infants. The diagnosis is usually made by roentgenogram. The prognosis in infants is usually good. Many recover quickly.

KRUPINSKI, Chicago.

Diseases of the Gastrointestinal Tract, Liver and Peritoneum

THE NORMAL GASTRIC SECRETION OF INFANTS AND SMALL CHILDREN FOLLOWING STIMULATION WITH HISTAMINE. R. D. CUTTER, J. Pediat. **12**:1 (Jan.) 1938.

The purpose of this investigation was to obtain normal standards of gastric secretory volume and acidity following stimulation with histamine in children below 4 years of age and to outline a method of gastric analysis which would lend itself to clinical application and interpretation at this period of life. Seventy-two children (36 boys and 36 girls) between the ages of 4 days and 4 years who were in the pediatric service of Stanford University Hospital were studied. Some of the children included in the group were recovering from gastrointestinal disturbances, but no child was included whose hemoglobin was below 70 per cent (Sahli) (12 Gm. per hundred cubic centimeters of blood). The method used is described in detail.

The gastric juice of the very young subjects was thick, mucoid and somewhat opaque, whereas that of the older children was usually clear and almost watery. Scatter diagrams are presented, showing the range of values obtained for gastric secretory volume, total acidity, free acidity and p_H. The range of normal values for gastric volume and acidity was wide. The gastric volume and acidity showed rapid increase during the first year of life and slower increase thereafter. The increase in volume during the first four years was found to be proportional to growth as measured by body weight.

RAUH, Cincinnati.

HERPETIC STOMATITIS. K. DODD, L. M. JOHNSTON and G. J. BUDDINGH, J. Pediat. **12**:95 (Jan.) 1938.

There has been great confusion in the literature, including pediatric textbooks, as to the status of stomatitis. This report is a bacteriologic study of 12 cases of stomatitis in a form identical with that described in most of the textbooks as aphthous stomatitis. Material from the lesions was inoculated into the corneas of 12 rabbits, and in each instance there was produced a purulent keratoconjunctivitis typical of herpes simplex. The infected corneas of 9 of the 12 rabbits showed typical intranuclear herpetic inclusions. Immunity to a known strain of herpes simplex was demonstrated in 6 of 7 rabbits which survived the infection. The authors conclude that this type of stomatitis is a definite clinical entity with the virus simplex as the causative agent and should be designated as herpetic stomatitis. Since in most cases it occurs in children, it probably represents a primary herpetic infection.

RAUH, Cincinnati.

GASTRO-INTESTINAL PATHOLOGY IN INFANCY. S. GIBSON, M. Clin. North America **22**:153 (Jan.) 1938.

One case each of hypertrophic stenosis of the pylorus, pylorospasm, intussusception and Meckel's diverticulum are described, with notes on diagnosis and treatment.

EUGENE H. SMITH, Ogden, Utah.

TWO CASES OF CONGENITAL MICROCOLON. J. B. EWING and W. E. COOKE, Brit. J. Surg. **25**:506 (Jan.) 1938.

Congenital narrowing of any portion of the intestinal tract of a degree sufficient to cause symptoms is uncommon. It is computed that it is observed in about 1 in 500,000 autopsies.

Two cases are reported that occurred within a period of twelve months, both in boys aged 3 days. In both these patients there were absolute constipation, abdominal distention and vomiting. A mass could be palpated in the abdomen. Pathologically there was narrowing of the ileum immediately above the cecum, which measured 9 mm. in diameter. Microscopically the muscular wall of the ileum was hypertrophied but the mucosa was normal. The colon measured 5.5 mm. and had hypertrophy of its muscular coat. There was no meconium in the colon. There was no constriction in any part.

Theoretically congenital microcolon is caused by lack of relaxation—an achalasia—due to a defect in the autonomic nervous mechanism. The anatomic structure is normal, but meconium has not passed into the colon because it has never opened to receive it.

SUMMERFELDT, Toronto, Canada.

EFFECT OF ENTERAL AND PARENTERAL INFECTION AND INTOXICATION ON THE SMALL INTESTINES. H. O. HETTCHE, Arch. f. Hyg. **119**:13 (Jan.) 1938.

Hettche employed as experimental animals guinea pigs anesthetized with ethyl carbamate (urethane). A cannula was inserted into the small intestine and pressure reading indicating peristaltic activity taken with a manometer connected with the cannula. Botulinus toxin administered to the point of causing death of the animal did not affect the motor activity of the intestine. Diphtheria toxin and diphtheria bacilli caused a transient increase in irritabilty of the bowel just before death. Infecton with Breslau bacteria caused a diminution in irritability of the bowel just before death, which was not dependent on the amount of bacteria. In contrast to morphine and prostigmin, the aforementioned agents do not cause a diminution in the irritability of the bowel but only a change in the hydrostatic pressure necessary to cause peristalsis.

GLASER, Rochester, N. Y.

MIXED TUMORS OF THE PAROTID GLANDS AND THE SURGICAL SIGNIFICANCE OF THE ECTOPIC FORMS. F. GRIBEL, Deutsche Ztschr. f. Chir. **249**:673, 1938.

Gribel reviews a series of 84 cases of mixed tumor of the parotid gland, in 23 of which the growth was outside the main body of the gland. Such a tumor is simple to recognize clinically and because of its delimitation by a fibrous capsule is easy to enucleate. In general the mixed tumor is benign although characterized by a tendency to recur. In some cases a growth of long standing may undergo malignant degeneration; therefore it is necessary to remove the mixed tumor at an early age. The principal location of such a tumor is in the palate.

GLASER, Rochester, N. Y.

PARTIAL ALIMENTARY INTOXICATION. A. VON SZASZ, Monatschr. f. Kinderh. **72**:394 (March) 1938.

Von Szasz briefly reviews her clinical material and comes to the conclusion that acute acidosis with vomiting and acetonuria in the runabout child is simply

a modified form of Finkelstein's alimentary intoxication. As the child gets older, the diarrheal symptoms become less pronounced and the metabolic disturbance less marked.

GERSTLEY, Chicago.

THE MANNER OF ACTION OF THE APPLE DIET. A. Voss, Ztschr. f. Kinderh. **59**:391 (Dec. 24) 1937.

Most reports regarding the action of the raw apple diet place in the foreground the chemical and physical properties of the pectins. Voss stresses the mechanical aspects of this diet. Absorption of water by cellulose and pectin causes the ingested apple to become bulky and to distend the intestinal wall. Distention of the intestinal wall provides the stimulus for normal peristalsis. In accordance with the "law of the intestine" (Bayliss and Starling) the tonicity of the intestine increases above and decreases below the distended portion. Since small feedings furnish too little bulk, large feedings should be given. Greater bulk also assures better cleaning out. Roentgenologic studies with raw apple and substitutes showed raw apple to be the most effective (plates are presented). Infants are alleged to be less amenable to the raw apple therapy than older children.

SIEMSEN, Chicago.

PERFORATION OF THE DUODENUM IN CHILDHOOD. M. DOBAY, Orvosi hetil. **81**:1042 (Oct. 9) 1937.

A 15 year old boy was admitted to the surgical clinic in Debreczen, Hungary, because of pains in the stomach for five months, sometimes accompanied for a short time by heart burn. The child did not attach great importance to these pains and did not mention them even to his parents. Two weeks before his admission to the clinic he felt great spasms and pains in the region of his stomach; on the last day, during his dinner, he experienced a bad spasm and vomited. The physicians thought that he had appendicitis, and an immediate operation was performed. Only then did it become evident that the duodenum was perforated. The operation brought about complete recovery. In the following four years the child gained 11 kg. and did not have any digestive disorders. Perforation of a duodenal ulcer is rare in childhood. Redwitz could collect only 100 instances from the literature.

GÖTTCHE, Budapest, Hungary.

Nervous Diseases

MENTAL CHANGES FOLLOWING THE REMOVAL OF THE RIGHT CEREBRAL HEMISPHERE FOR BRAIN TUMOR. STUART H. ROWE, Am. J. Psychiat. **94**:604 (Nov.) 1937.

A woman aged 38, suffering from a tumor of the brain, had the right cerebral hemisphere removed in three consecutive stages. There was general improvement in her physical and mental status. The case substantiates "previous experimental and clinical studies which indicate that in primates and man the higher cerebral functions are more severely altered by bilateral frontal lobe injury than by corresponding or even more extensive lesions of any other areas."

JAHR, Omaha.

EPIDEMIC ENCEPHALITIS. W. L. HOLT JR., Arch. Neurol. & Psychiat. **38**:1135 (Dec.) 1937.

This report deals with a follow-up study of 266 cases in which the diagnosis of epidemic encephalitis was made. Nearly all the patients had their illness following 1917. Of the entire number, 11.5 per cent were found to be alive and without known sequelae after from ten to sixteen years. Seventy-two patients with sequelae had a recovery rate of 1.4 per cent. Holt concludes: "Children with

behavior disorders constitute the only group with sequelae of epidemic encephalitis in whom improvement may reasonably be expected."

BEVERLY, Chicago.

FACTORS PRODUCING LUMBAR CEREBROSPINAL FLUID PRESSURE IN MAN IN THE ERECT POSITION. T. J. C. VON STORCH, E. A. CARMICHAEL and T. E. BANKS, Arch. Neurol. & Psychiat. **38**:1158 (Dec.) 1937.

In studying cerebrospinal fluid pressure in man, the authors conclude that the normal pressure of a person in the sitting position bears no relationship to the normal pressure of that person in the recumbent position. They also found that the pressure in the sitting position is roughly equivalent to the vertical distance between the cisterna magna and the point of puncture.

BEVERLY, Chicago.

A CLINICOPATHOLOGIC STUDY OF ASTROCYTOMAS. R. W. WAGGONER and K. LÖWENBERG, Arch. Neurol. & Psychiat. **38**:1208 (Dec.) 1937.

Astrocytoma of the cerebrum differs from that of the cerebellum. Starting from a nucleus, it invades and destroys myelinated tracts. The extension depends on the position of the initial nucleus. Bilateral invasion occurs when the nucleus is in the corpus callosum, the direction depending on the part involved. Unilateral astrocytoma of the cerebrum may involve the whole hemisphere or a part of it.

BEVERLY, Chicago.

CHANGES IN THE BRAIN OF PLEXECTOMIZED DOGS, WITH COMMENTS ON THE CEREBROSPINAL FLUID. G. B. HASSIN, E. OLDBERG and M. TINSLEY, Arch. Neurol. & Psychiat. **38**:1224 (Dec.) 1937.

The authors repeated the experimental work of Dandy, in which he attempted to determine in dogs the effect of removal of the choroid plexus and especially to determine the relationship of the choroid plexus to the cerebrospinal fluid. They concluded: "Experimental plexectomy does not give uniform results—the plexectomized ventricles may be smaller than the normal ventricle, the same size or even larger. The size may be affected by large scars that result from operative procedures. Both pathological and experimental data indicate that cerebrospinal fluid forms in the ventricles, but not from the choroid plexus. It comes only from the cerebral tissue fluids drained by the ventricles (through the connecting Virchow-Robin channels). The presence of external hydrocephalus denotes the existence of an additional draining system (in the subarachnoid space), which is of the same anatomicoclinical significance as internal hydrocephalus."

BEVERLY, Chicago.

MIGRAINE IN CHILDREN AND THE MECHANISM OF THE ATTACK. HENRY ALSOP RILEY, Bull. Neurol. Inst. New York **6**:387 (Dec.) 1937.

Migraine in children is not uncommon. It has been estimated that in 80 per cent of cases migraine begins in childhood. Eight cases in which the patients were under 13 years of age have been encountered in the migraine clinic of the Neurological Institute of New York. The age varied from 2 to 13 years. The symptoms were the same as in adults except that none had hemianopia and the visual disturbances were more pronounced. They were all increased by excitement.

The author discusses abdominal symptoms of the type associated with migraine both with and without headache. "In any child presenting symptoms of an obscure character located in the abdomen, careful investigation should be made into the past and family history in order to determine the presence of any tendency toward the development of migrainous episodes."

The author includes an excellent detailed description of the causation and mechanism of migraine. It is apparently a localized disturbance accompanied by

either vasodilatation or vasoconstriction, causing a pain by stimulation of the nerve ends in the walls of the blood vessels, especially the larger arteries.

BEVERLY, Chicago.

PYOGENIC INFECTIONS WITHIN THE VERTEBRAL CANAL. M. MADISON CAMPBELL, Bull. Neurol. Inst. New York **6**:574 (Dec.) 1937.

The author reports 8 cases of pyogenic infection within the vertebral canal. The symptoms present wide variations and diverse manifestations. There is usually a history of primary pyogenic focus elsewhere in the body. The symptoms referable to the spinal cord may be acute or mild; the temperature may range from 100 to 106. Malaise, headache, vomiting, blurring of vision, convulsions, myoclonia, anesthesia and hyperalgesic bands, with gradually developing muscular weakness sometimes progressing to complete paraplegia with urinary and fecal incontinence, are commonly found.

Laminectomy as an emergency measure immediately after the establishment of the diagnosis is recommended.

BEVERLY, Chicago.

STREPTOCOCCIC MENINGITIS, WITH SPECIAL EMPHASIS ON SULFANILAMIDE THERAPY. WALTER H. TRACHSLER, GEORGE S. FRAUENBERGER, CARL WAGNER and A. GRAEME MITCHELL, J. Pediat. **11**:248 (Aug.) 1937.

In 1935 Gray reported from the literature 66 cases of streptococcic meningitis, in which recovery occurred. The authors add reports of 39 similar cases collected from the literature and reports of 5 cases of their own. They review the methods of treatment used in these 110 cases and give detailed histories of their own cases. From 1927 to Jan. 1, 1937, 14 patients with streptococcic meningitis were treated in the Children's Hospital, with only 1 recovery. During the first five months of 1937, 7 patients were treated in this institution, with 4 recoveries. These patients were all treated with sulfanilamide. Because of the use of blood transfusions, antistreptococcus serum and parenteral fluids in these 7 cases in addition to the sulfanilamide therapy, no suggestion is made as to the possible effect of this drug alone, but the high percentage of recovery gives a favorable impression of the effect of this drug in cases of streptococcic meningitis.

RAUH, Cincinnati.

DURAL SINUS THROMBOSIS IN EARLY LIFE: I. THE CLINICAL MANIFESTATIONS AND EXTENT OF BRAIN INJURY IN ACUTE SINUS THROMBOSIS. O. T. BAILEY and G. M. HASS, J. Pediat. **11**:755 (Dec.) 1937.

The present study deals with the clinical and pathologic observations in 80 cases of thrombosis of the dural sinuses in infancy and childhood. In 42 of these cases the thrombosis was associated with various forms of sepsis, meningitis, scalp infections, otitis media, mastoiditis and bacteremia without meningeal localization. In 4 cases it followed surgical procedures. The greater part of this study concerns itself with 33 cases of acute sinus thrombosis unassociated with sepsis or surgical procedures. All the patients were less than 30 months of age. The illness began with an acute nutritional disturbance, usually followed after a period of days or weeks by evidence of meningeal irritation, marked hyperpyrexia and convulsions or other abnormal neurologic manifestations. Some infants died without any evidence of neurologic disturbance. In all these patients the superior longitudinal sinus was thrombosed in its entirety or in part, with variable involvement of other sinuses and cerebral veins. Twenty-one of the patients presented hemorrhages into the meninges, associated in 19 cases with intracerebral hemorrhage and necrosis. Some of the patients succumbed within a few hours after the onset of the symptoms referable to involvement of the central nervous system. A few lived for from ten days to one month. Two patients recovered from

their acute attacks and died later with organized and canalized thrombi in their superior longitudinal sinuses. This "nonseptic" thrombosis of the dural sinuses has no counterpart in adult life and largely accounts for the much greater incidence of thrombosis of the dural sinuses in early life than in adult life.

RAUH, Cincinnati.

INTRACRANIAL HEMANGIOMA ASSOCIATED WITH FACIAL NEVUS. A. O. HECKER, J. Pediat. **11**:797 (Dec.) 1937.

The terms "naevoid amentia" and "encephalotrigeminal angiomatosis" have been applied to a syndrome the outstanding manifestations of which are: a port wine nevus of the face associated with homolateral intracranial hemangioma, epilepsy, paralysis and mental retardation. Hecker adds 2 more cases to the 84 reported in the literature. He reproduces roentgenograms of the skull of one of the patients, showing a calcified intracranial hemangioma. He is of the opinion that the motor and psychic phenomena found in this syndrome are secondary to the intracranial hemangioma and are due to the same factors which produce motor and psychic phenomena in instances in which other intracranial tumors can be demonstrated or to other factors which produce destruction or faulty function of brain cells. He believes that in some of the cases a primary mental deficiency may also be present which adds to the severity of the objective mental responses.

RAUH, Cincinnati.

THE DIAGNOSIS AND TREATMENT OF OTITIC MENINGITIS. JAMES G. ARNOLD JR., M. Clin. North America **21**:1313 (Sept.) 1937.

The most common cause of meningitis, excluding the meningococcic and the tuberculous forms, is otitic infection. The local symptoms of the otitic involvement may be masked or evident, but of the greatest importance is the early recognition of the signs and symptoms of meningeal irritation. These may occur early or late in the course of the otitic infection and do not differ materially from meningeal symptoms from other causes. At the earliest possible moment it should be determined whether the meningeal reaction is sterile or the result of actual infection of the subarachnoid space. If the former, relief of pressure by spinal drainage and eradication of the infectious focus may bring about prompt disappearance of symptoms. Recovery from true infective otitis meningitis is a rarity. Cultures should be made at the time a paracentesis is done and at also every mastoid operation, in order that the infecting agent may be known should meningitis supervene. Sterile meningitis should be treated by prompt exploration of the mastoid and by spinal drainage. The administration of hypotonic dextrose solutions before drainage will increase the flow of spinal fluid. Arnold's experience with sulfanilamide in the treatment of meningitis due to the hemolytic streptococcus has been favorable. He advises its use in all cases in which the disease is due to this organism and also in cases in which the infecting organism is not known. In dealing with streptococcic meningitis when sulfanilamide therapy is used, the advisability of doing a mastoidectomy is an open question. If the original otitic infection is due to an organism other than the hemolytic streptococcus and the meningitis is still in the sterile stage mastoidectomy should be done as early as possible.

EUGENE SMITH, Ogden, Utah.

THE LUMBAR PUNCTURE PRESSURES IN SUBARACHNOID HEMORRHAGE. R. KEMP, Lancet **2**:1369 (Dec. 11) 1937.

The most striking way in which a subarachnoid hemorrhage may arise is by bleeding from a "congenital aneurysm" in a comparatively young person. The body mechanism usually saves the patient's life by a spontaneous clotting inside the bleeding sac. There is still little known about the factors which determine recovery.

Only occasional manometric readings were recorded throughout the course of illness of 9 patients, but they showed that most of the symptoms are not associated with raised thecal tension and are not the result of it.

LANGMANN, New York.

ANATOMOCLINICAL STUDY OF A CASE OF CHOREA MOLLIS. G. MARINESCO, S. DRAGANESCO, S. AXENTE and I. BRUCKNER, Ann. de méd. **40**:397, 1936.

This rare disease, which has been described by West as limp chorea and by Gowers as chorea paralytica, does not present any definite pathologic changes in the central nervous system but is associated with degenerative changes of the striated muscles. The authors describe the case of a girl aged 15, who one year before admission to the hospital had suffered from rheumatic arthritis. About one month before admission her movements became incoordinate; gradually choreiform movements appeared in both the face and extremities. The tendon and cutaneous reflexes disappeared, but sensation was not affected. The choreiform movements disappeared gradually and were followed by flaccid paralysis of the extremities. Severe septicemia developed, and the patient died ten days after admission.

Autopsy revealed acute swelling of the spleen, fatty degeneration of the liver, glomerulonephritis, pericarditis and endocarditis, with severe lesions of the mitral valves and fatty degeneration of the cardiac muscle. The muscles of the extremities showed fatty degeneration, together with perivascular lymphocytic infiltration and complete disappearance of glycogen. In the spinal cord there was mild myelitis, with acute changes in the ganglion cells. The histologic lesions of the brain were vague: widespread chromatolysis of neurons and mild satellitosis within the basal ganglions, without marked disease of the neurons. Besides, there was mild distention of the meningeal veins, with scattered, minute perivascular hemorrhages and mild lymphocytic infiltration.

The authors discuss the relative significance of these pathologic changes in view of the clinical manifestations of choreiform movements. They emphasize the widespread pathologic alteration of the central nervous system without predilection for any single nucleus, a fact which does not support the idea of localization of the morbid process in the neostriatum. The transformation of active chorea into chorea paralytica in this case can be explained by the myositis and the degenerative changes in the striated muscle fibers, but not by a lesion of the central nervous system.

WIEL, Chicago. [ARCH. NEUROL. & PSYCHIAT.]

A STUDY OF CEREBRAL TUMORS IN THE CHILD. L. BABONNEIX, Arch. de méd. d. enf. **40**:761 (Dec.) 1937.

Cerebral neoplasms appear to be more frequent in the young as well as among adults than formerly. Babonneix has assembled histories of a number of personal observations and attempts, in comparing these, to draw some practical conclusions.

The initial symptoms of cerebral tumors may involve the digestive system, in which event there is vomiting, localized abdominal pain, anorexia and disturbances of intestinal function severe enough to suggest appendicitis. Three illustrative cases in which the condition had such an onset are reported. In other invasions the symptoms are frankly cerebellar; a syndrome pointing to involvement of the area of the infundibulum and tuber cinereum may be a confusing factor.

Among the various tumors considered are: pontocerebellar tumor, craniopharyngioma, intraprotuberantial tumor, angioma of the meninges, astrocytoma, ependymoglioma, medulloblastoma and cerebellar tuberculoma.

Under diagnosis Bebonneix especially stresses examination of the eyes for papillary stasis, careful investigation of vomiting attacks and early roentgen and ventriculographic studies.

AMESSE, Denver.

PREVENTION OF CONVULSIONS IN CHILDREN. WALTER PEIRIS, Bull. Assoc. internat. de pédiat. prevent. **4**:10, 1937.

Convulsions occurring in very young subjects constitute one of the major problems of the pediatrician and the general practitioner; as a matter of fact, they attend the most frequent sources of mortality in early infancy, and the most profound study is necessary to determine whether such symptoms are idiopathic, organic, metabolic, chemical, toxic, reflex or hysterical.

The development of broad approach in these conditions will tend to give a clearer view of the diverse and variable reactions of the central nervous system and of the possibilities of a cerebral lesion, latent or unsuspected. From 40 to 50 per cent of stillbirths and of neonatal deaths are due to trauma, while among children who survive such accidents many will be subject to convulsive crises. Investigation of the primary cause, then, should take precedence over the consideration of secondary sources. The prevention of trauma through adequate observation during the antenatal period together with the application of well known rules of hygiene will serve to minimize the incidence of convulsive disorders.

AMESSE, Denver.

SECONDARY PNEUMOCOCCIC MENINGITIS IN AN INFANT. E. HURMUZACHE and D. WEISBUCH, Bull. Soc. de pédiat. de Iasi **7**:94 (Oct.-Dec.) 1936.

A poorly nourished infant aged 16 months had pneumonia. Crepitant rales were found at the base of the right lung, and the child showed extreme dyspnea. Nine days later the dyspnea was accentuated, stiffness of the neck developed, the Kernig sign was present, and the fontanel bulged. The spinal fluid showed 308 cells, with numerous gram-positive diplococci. The child died two days later. Autopsy showed nodules of bronchial pneumonia at the base of the right lung, pneumococcic meningitis and also pyelonephritis.

LESLIE, Evanston, Ill.

PURULENT MENINGITIS OF UNDETERMINED ORIGIN IN A TWO MONTHS OLD INFANT. GRACOSKI and E. HURMUZACHE, Bull. Soc. de pédiat. de Iasi **7**:98 (Oct.-Dec.) 1936.

A 2 month old infant had fever and convulsions. The convulsions numbered from eight to ten a day and decreased in frequency, disappearing at the eighth day. The spinal fluid was at first very cloudy, with numerous cells, which were predominantly polymorphonuclear. Complete clinical recovery took place ten days from the onset. The changes in the spinal fluid persisted for thirty days. At no time were any organisms found in the spinal fluid either on smear or on culture.

LESLIE, Evanston, Ill.

PARALYSIS OF THE BRACHIAL PLEXUS AND PARALYSIS OF THE DIAPHRAGM. H. GRENET, P. ISAAC-GEORGES and LADET, Bull. Soc. de pédiat. de Paris **35**:146 (Feb.) 1937.

Two cases of injury to the brachial plexus resulting in paralysis of the upper extremity as well as of the diaphragm are reported. Both patients were infants. A needle was inserted at the base of the right lung in 1 case, as a collection of pleural fluid was thought to be present. The physical signs were due, of course, to elevation of the liver.

BENJAMIN, Montreal, Canada.

METASTATIC ABSCESS OF THE BRAIN AND PULMONARY SUPPURATION DUE TO THE PRESENCE OF A GRASS STEM. CASSOUTTE, CAPUS and R. BERNARD, Bull. Soc. de pédiat. de Paris **35**:193 (March) 1937.

A boy aged 6 years had pulmonary bronchiectatic infection caused by a foreign body. He died of a cerebral abscess three days after operation was performed for the pulmonary condition.

BENJAMIN, Montreal, Canada.

A Large Meningoencephalocele; Excision; Cure. Paul Giraud and J. Boudouresque, Bull. Soc. de pédiat. de Paris **35**:287 (May) 1937.

A boy was born with a large meningoencephalocele. At the age of 1 month he was operated on, local anesthesia being used, and a mass weighing 500 Gm. was removed. When seen again at the age of 3 months he appeared normal, but the head measured 42 cm. in circumference (normal 39 cm.), although there were no signs of hydrocephalus. The mass was lined by a thick neuroectodermal tissue of neuroglial appearance, and there was a richly vascular perineural connective tissue which resembled meninges.

Benjamin, Montreal, Canada.

Cerebral Tumor: Report of a Case. L. Babonneix and Delaitrie, Bull. Soc. de pédiat. de Paris **35**:380 (June) 1937.

A girl aged 11 showed signs and symptoms of a tumor of the brain which had begun three months previously. Necropsy revealed a malignant neoplasm which was attached to the left mastoid. A definite histologic diagnosis was not made; the tissue resembled myelosarcoma.

Benjamin, Montreal, Canada.

Suppurative Streptococcic Meningitis with Recovery in Children: Report of Two Cases. Robert Clément and Madeleine H. Salembiez, Bull. Soc. de pédiat. de Paris **35**:397 (June) 1937.

A boy aged 8 had streptococcic meningitis twelve days after the onset of scarlet fever. He was given antistreptococcus serum intrathecally and intramuscularly on the fourth day after the beginning of meningitis. He recovered. A girl aged 3 years had purulent meningitis and was treated with antimeningococcus serum. A slowly growing streptococcus was isolated in a culture from the spinal fluid. When injected intravenously into a rabbit, the organism did not produce rapidly fatal septicemia. The girl recovered. It is possible that the strain of Streptococcus in each of these cases may have been not highly virulent and that the resistance of the children was strong.

Benjamin, Montreal, Canada.

Postencephalitic Torsion Spasm. Divry and E. Evrard, J. belge de neurol. et de psychiat. **37**:179 (March) 1937.

Divry and Evrard describe the pathologic changes in the case of a feeble-minded boy aged 17, who had had torsion spasm of the neck since the age of 13. He had also shown rigidity of the spine and of the upper extremities, especially on the left, and, to a lesser extent, of the lower extremities. The clinical picture resembled that of decerebrate rigidity; tonic neck reflexes were present.

Study of the brain showed evidences of parenchymatous degeneration and glial scarring in the substantia nigra, with remnants of former perivascular infiltration. There were Alzheimer cell changes in the substantia nigra and the quadrigeminal bodies. The pathologic changes involved the pallidum and infundibulum, but the maximal change was in the mesencephalon. The authors believe that the process is encephalitic, but state that it is unusual for one to find lesions so similar to those observed in postencephalitic parkinsonism without clinical signs of parkinsonism. They stress the correlation between the lesions in the mesencephalon and the symptoms of decerebrate rigidity and call attention to the fact that mental deterioration may follow a postencephalitic torsion spasm.

Waggoner, Ann Arbor, Mich. [Arch. Neurol. & Psychiat.]

CONGENITAL DISTURBANCE OF ASSOCIATED MOVEMENTS OF LATERALITY (STILLING'S SYNDROME): CONSIDERATIONS ON THE VESTIBULAR EXAMINATION. E. AUBARET, G. E. JAYLE and G. FARNARIER, Rev. d'oto-neuro-opht. **15**:33 (Jan.) 1937.

On the basis of the study of a case of their own and of several cases reported by others, Aubaret and his associates believe that Stilling's syndrome is not always of peripheral origin. This syndrome is characterized by congenital monocular absence of movements of laterality, enophthalmos and movements of sursumvergence when the abolished function is attempted. The case reported is that of a boy aged 9 years, with congenital convergent strabismus of the right eye. There was slight enophthalmos of the left eye. When he looked to the left, the left eye did not pass the median line and the enophthalmos was increased. When he looked to the right, the left eye executed movements of sursumvergence. Convergence was made only with the right eye. The pupillary reflex in accommodation was abolished, and the reflex to light was maintained in the left eye. Vestibular stimulation by rotation produced normal responses from the right eye; in the left eye there was no nystagmus to the left. Transformation of the lateral movement into sursumvergence permits establishment of a semeiologic chain between strabismus with sursumvergent deviation in certain cases and complete paralysis of lateral movement; both conditions are congenital. If Stilling's syndrome leads by successive transitions to strabismus with sursumvergent deviation, it leads also to simple concomitant strabismus, the intermediary step being congenital paralysis of the external oculomotor nerve, with the addition of strabismus of the opposite eye. These facts support the theory of the frequent, if not constant, central origin of the syndrome. Further support is furnished by the history of certain paralyses of movement of the globe which shows that a cerebral lesion may cause signs identical with those observed in Stilling's syndrome: oculopalpebral synkinesis and enophthalmos in cases of paralysis of lateral movements and replacement of provoked vestibular movements of laterality by movements of sursumvergence. The fact that atrophy of the internal and external rectus muscles occurs is not an argument for a peripheral lesion, for a central lesion may be followed by degeneration of the muscles.

DENNIS, San Diego, Calif. [ARCH. NEUROL. & PSYCHIAT.]

RECENT ADDITIONS TO THE TREATMENT OF PETIT MAL IN CHILDREN. G. SANPAOLESI, Lattante **8**:182 (April) 1937.

Two patients with petit mal were successfully treated by the ketogenic diet.

HIGGINS, Boston.

TUMOR OF THE SPINAL CANAL. G. GUASPARI, Riv. di clin. pediat. **35**:865 (Oct.) 1937.

Guaspari reports a case in which a boy aged 7 years had a tumor in the spinal canal. The tumor was a hemangioendothelioma and originated from the periosteum of the right lamina of the fourth dorsal vertebra. The clinical symptoms were pain and intermittent spastic paraplegia of the legs. The tumor was the size of a walnut and weighed 10 Gm. The child died at operation; death was probably the result of status thymicolymphaticus, which was revealed at autopsy.

HIGGINS, Boston.

CEREBRAL TREMORS IN AN INFANT. C. PERNETTA, J. de pediat., Rio de Janeiro **4**:564 (Dec.) 1937.

A 9 year old boy began to have generalized tremors of the extremities, hypertonic musculature and exaggerated tendon reflexes. The spinal fluid was

normal. The author considered this condition to be postinfectious encephalitis. He believes that the virus was present before the infection and obtained a foothold in the organism when this was weakened by the disease.

SANFORD, Chicago.

THERAPEUTIC USE OF IODIZED POPPYSEED OIL IN TREATMENT OF CEREBRAL AND CEREBELLAR ABSCESSES. B. KARBOWSKI, Monatschr. f. Ohrenh. **70**:1044 (Sept.) 1936.

The fact that in cases of pulmonary abscess the introduction of iodized poppyseed oil is often followed by improvement or cure induced Karbowski to try this substance in treating abscess of the brain when the postoperative course was not satisfactory. He reports 2 cases. He ascribes the favorable influence of iodized poppyseed oil on the postoperative course of abscesses of the brain to the strongly disinfecting action of the substance, with its 40 per cent iodine content, and to the favorable effect of the fat on ulcerating surfaces. Moreover, the high specific gravity of the substance facilitates the evacuation of the abscess, because the suppurating exudate gathers above it. The 2 cases observed by the author indicate that fillings of iodized poppyseed oil are well tolerated. The resorption of the substance is extremely slow.

EDITOR'S ABSTR. [ARCH. OTOLARYNG.]

DEGENERATIVE ENCEPHALOPATHY IN INFANTS AND CHILDREN AT BATAVIA. W. J. C. VERHAART, Acta pædiat. **20**:107, 1937.

Verhaart describes the anatomic changes in 41 Chinese infants who died after illnesses characterized by fever, vomiting, diarrhea, convulsions and stupor. In all instances epidemic encephalitis had been suspected during life. The histologic alterations in the central nervous system were those of nonspecific "toxic" encephalitis; they consisted principally of degenerative changes in the parenchyma, with proliferative phenomena in the supporting structures and in the blood vessels.

McCUNE, New York.

OPERATIVE TREATMENT OF ENCEPHALOCELE AND MENINGOCELE. F. VERBEEK, Maandschr. v. kindergeneesk. **7**:1 (Oct.) 1937.

After a short discussion of different methods of surgical treatment of encephaloceles and meningoceles, the author gives an extensive description of Penfield's method and recounts the results obtained by this method with 13 children. Photographs of the children, taken before and after the operation, are presented.

VAN CREVELD, Amsterdam, Netherlands.

THE LUMBAR PUNCTURE AS A THERAPEUTIC MEASURE. A. BIEMOND, Nederl. tijdschr. v. geneesk. **81**:3447 (July 17) 1937.

The therapeutic significance of lumbar puncture is small as compared with its great diagnostic value. It may act favorably in cases of intra-arachnoid hemorrhage, but in cases of ruptured aneurysm one runs the risk of an aggravation of the hemorrhage. The therapeutic value of lumbar puncture in meningitic processes is mainly based on its effect of lessening the tendency toward adhesions. A remarkably good effect may be obtained in cases of benign lymphocytic meningitis. As a pressure-relieving measure, lumbar puncture hardly comes into consideration on account of its temporary effect; moreover, in all cases of cerebral tumor it is more or less dangerous and therefore inadvisable.

VAN CREVELD, Amsterdam, Netherlands.

MENINGISM IN LEUKEMIA AND IN WEIL'S DISEASE. J. E. MINKENHOF, Nederl. tijdschr. v. geneesk. **81**:4448 (Sept. 18) 1937.

Some patients are described as showing meningism. The first patient suffered from subacute lymphatic leukemia, which presented as it progressed the complete picture of meningococcic sepsis with meningitis. A brief review is added of the neurologic changes associated with leukemia. The other patients suffered from Weil's disease, the only signs of which were pyrexia and meningeal irritation. The composition of the cerebrospinal fluid of patients with the various forms of Weil's disease are discussed.

VAN CREVELD, Amsterdam, Netherlands.

SALAAM CONVULSIONS. J. J. H. M. KLESSENS, Nederl. tijdschr. v. geneesk. **81**: 4566 (Sept. 25) 1937.

A boy aged 4 years had a series of salaam convulsions daily; he was of normal build and was only slightly backward mentally. Cure resulted in a few days after he was placed on a ketogenic diet.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of the Genitourinary Tract

FURTHER OBSERVATIONS ON THE TREATMENT OF HYPOGENITALISM AND UNDESCENDED TESTES, WITH SPECIAL REFERENCE TO THE PRODUCTION OF PREMATURE PUBERTY. W. O. THOMPSON, N. J. HECKEL, P. K. THOMPSON and L. F. N. DICKIE, Endocrinology **22**:59 (Jan.) 1938.

The value of the gonadotropic principle from the urine of pregnant women in the treatment of undescended testes and hypogenitalism is confirmed. In 8 of 36 patients with undescended testes complete descent was secured within nine weeks. One of the most striking results was the genital growth.

JACOBSEN, Buffalo.

TREATMENT OF NEPHROSIS IN THE YOUNG CHILD. F. W. SCHLUTZ and J. L. COLLIER, J. A. M. A. **109**:1959 (Dec. 11) 1937.

The authors discuss the various forms of treatment that have been used for nephrosis and describe thoroughly the rationale and technic of the alkali treatment. In many cases, particularly those of the acidemic type, the edema and proteinuria can be relieved by forceful alkali therapy carefully controlled by determinations of plasma bicarbonate and of the urinary alkalinity. Of the authors' 7 patients 3 recovered and 4 died of complications.

HEERSMA, Kalamazoo, Mich.

LYMPHOGRANULOMA VENEREUM IN CHILDHOOD: REVIEW OF THE LITERATURE WITH REPORT OF A CASE. H. LEVY, J. Pediat. **11**:812 (Dec.) 1937.

Lymphogranuloma venereum occurred in a 6 year old colored girl. The only objective symptoms were inguinal adenopathy, a scanty foul-smelling vaginal discharge and urethral inflammation. There were no symptoms referable to the rectum. The Frei test became positive four weeks after the onset. For both parents the Frei test was markedly positive, and they had definite lesions of lymphogranuloma venereum. From the literature Levy collected 9 other cases in children and he presents an analysis of these cases. The etiologic features, transmission, pathologic aspects, course, treatment and prognosis of lymphogranuloma venereum are discussed.

RAUH, Cincinnati.

A Follow-Up Study of Thirty-One Cases of Acute Infection in Female Children. L. R. Wharton and L. A. Gray, South. M. J. **31**:68 (Jan.) 1938.

Wharton and Gray present results of a follow-up study of 31 girls and young women who had acute urinary infections in infancy and childhood. From their study they conclude that in young girls acute urinary infections may not be dismissed as casually as they usually are. It is obvious that these infections in children exhibit the same characteristics as do those in adults and should therefore receive just as careful attention. One can be sure that in half of the cases the infections will clear up completely and permanently, even though the children have several attacks.

Neglect of urinary infections in childhood may lead to serious urologic disease in later life.

Schlutz, Chicago.

A Case of Pneumococcus Vaginitis Treated with the Anti-Serum. W. Bickers, Virginia M. Monthly **65**:104 (Feb.) 1938.

A child 9 years old with acute purulent vaginitis was found to have a local infection with Pneumococcus, type II. Vaginal treatment with ethylhydrocupreine base for a week caused no improvement. Type II antipneumococcus serum was instilled into the vagina and held there for one hour. Marked improvement followed within forty-eight hours. A second instillation was followed by disappearance of all signs of infection after another forty-eight hours.

Stone, Richmond, Va.

Use of Pituitary Preparations. P. M. F. Bishop, Practitioner **140**:38 (Jan.) 1938.

Descent of the testis appears to be governed by the luteinizing hormone. Spermatogenesis begins at the age of 9, and a testis imperfectly descended after this age tends to become functionless. Since the testes seem to be comparatively resistant to gonadotropic influences during extreme youth, it appears that the ideal time at which to treat cryptorchidism is between the ages of 7 and 12. Many imperfectly migrated testes may descend spontaneously during this period, but the fact that the condition is seen in adult life indicates that this does not always occur. If one testis is resident in the scrotum, virility is probably insured, but it is still important to encourage descent of the other, because a canal-dwelling testis is subject to injury and is said to be more liable to undergo malignant changes. If it is situated in the neighborhood of the external ring, attacks of pain may occur when it becomes engaged in the ring. Finally, if left untreated until the age of 12 or 14, it may become too large to pass through the external ring and then can be placed in the scrotum only by operation.

Treatment consists in the administration of the gonadotropic factor from the urine of pregnant women, in doses of from 100 to 500 to 1,000 rat units twice a week for from two to six months. In the majority of selected cases descent is achieved in from two to three months. Administration of high doses over a prolonged period may give rise to enlargement of the penis. This, however, is seldom alarming and is preferable to the alternative of an undescended testis. In some cases the testis tends to retract after it has been successfully lodged in the scrotum. Treatment should consequently be continued for two or three months after the scrotal position has been attained. The results of endocrine therapy in selected cases are good, and orchidopexy should be reserved for cases in which treatment with the gonadotropic substance mentioned is contraindicated or has failed.

Gelston, San Francisco.

Use of Female Sex Hormones in Treatment. D. Macleod, Practitioner **140**: 45 (Jan.) 1938.

Macleod deals with vulvovaginitis in children. In infection of the vagina by organisms, including the gonococcus, treatment with an estrogenic substance is

both rational and successful. Nabarro and Signy in 1935 reported that they had obtained excellent results and recommended the use of 4,000 units of the estrogenic substance daily, administered by mouth, accompanied by irrigation with a solution of iodine, 1 teaspoonful to the pint (4 cc. to 473 cc.). Enlargement of the breasts due to the activity of the estrogen is a constant feature. The average duration of treatment necessary to effect a cure varied from one to five months.

GELSTON, San Francisco.

USE OF MALE SEX HORMONES. E. W. RICHES, Practitioner **140**:60 (Jan.) 1938.

In man the testis descends during development, exchanging the warmer surroundings of the abdomen for the cooler environment of the scrotum, where its functions can be the better exercised. This descent is apparently stimulated by a gonadotropic hormone, and in many cases imperfect descent can be rectified by injections of the gonadotropic substance from the urine of pregnant women. Since 1930 a considerable number of cases in which this treatment was tried have been recorded in the literature, and success was attained in about 70 per cent of the total series of published cases. The recommended dosage is 500 rat units twice weekly, continued for from six to eight weeks if necessary. In many cases results are apparent after the second or third injection; if there is no result after three months, there should be, according to Spence (1936), a three month period of rest, as there is evidence of the production of an antihormone. Careful clinical examination is necessary at the outset to determine that the testis lies in a situation somewhere along its normal line of descent; if it does not, i. e., is ectopic, success is unlikely to result from treatment with the gonadotropic substance alone. Thompson in 1937 pointed out that failures may be due to shortness of the structures to which the cord and testis are attached or to abnormal fixity resulting from anatomic conditions. Even in such cases, however, the administration of the aforementioned gonadotropic substance will do much to make a subsequent orchidopexy easier and more certain through its effect of lengthening the structures of the cord, and after operation in a difficult case subsequent retraction may be prevented by the same means. Whether the condition is unilateral or bilateral, imperfect descent in an otherwise normal subject is often associated with a mechanical cause and is therefore unresponsive. Except in special cases it is wise to start treatment between the ages of 10 and 12 years; earlier treatment may lead to precocious sexual maturity, while undue delay will retard development.

GELSTON, San Francisco.

RENAL CALCULI AND VITAMIN METABOLISM. H. J. LAUBER, Med. Klin. **33**:1729 (Dec. 28) 1937.

Malnutrition, more especially vitamin deficiency, is important in the etiology of renal calculi. The relation between vitamin A deficiency and calculi in the bladder has been amply demonstrated experimentally. Epithelium damaged by vitamin A deficiency and infection may form the nucleus of a calculus. Vitamin A deficiency is accompanied by alkalinity of urine and probably by increased excretion of calcium. Vitamin B deficiency may cause a disturbance in calcium metabolism. Hematuria caused by vitamin A or vitamin C deficiency may lead to urinary stasis and the formation of calculi.

SIEMSEN, Chicago.

Diseases of the Ductless Glands; Endocrinology

CLINICAL USE OF CRYSTALLINE INSULIN. S. S. ALTSHULER, Ann. Int. Med. **11**: 901 (Dec.) 1937.

One hundred patients with diabetes mellitus, ranging in age from 6 to 86 years, were treated with crystalline insulin. The insulin was prepared according to the method of Dr. Melville Sahyum. Most of the patients required more than

two doses of insulin during each twenty-four hour period. Two of 10 patients under 20 years of age were controlled with one dose of insulin daily; the remainder required two doses at from ten to twelve hour intervals.

Reactions to the insulin were rare and when they occurred were not associated with much shock.

Much lower levels of blood sugar were obtained without manifest reactions than had been possible with regular insulin. READING, Galveston, Texas.

ADRENAL CORTICAL TUMOR: A REPORT OF FOUR CASES. C. H. LAWRENCE, Ann. Int. Med. **11**:936 (Dec.) 1937.

Lawrence reports 4 cases, 2 of which occurred in children, one a girl aged 13 years and the other a boy aged 14 years. The other 2 patients were adults aged 24 and 30 years, respectively.

The girl showed amenorrhea, masculinization, changes of voice and hypertrichosis. A tumor of the right adrenal was removed along with the right kidney. Improvement was noted a year later.

The boy presented obesity, one convulsive attack and dizzy spells. Necropsy revealed an adenoma of the anterior lobe of the pituitary and adrenal hypertrophy.

The details of each case are given. READING, Galveston, Texas.

EFFECTS OF INSULIN HYPOGLYCEMIA UPON THE DIABETIC HEART IN CHILDREN AND YOUTHS. H. F. ROOT, Ann. Int. Med. **11**:1332 (Jan.) 1938.

By electrocardiographic examination of 25 young persons who had diabetes Root found that insulin hypoglycemia produces no serious change in a normal heart. If the condition of the patient is complicated by coronary disease, a serious effect on the heart may result by reason of the adrenal stimulation which accompanies hypoglycemia. In the cases studied, bradycardia was as common as tachycardia. Proper use of insulin and of diet will prolong life in a patient with coronary disease complicating diabetes. READING, Galveston, Texas.

PRESENT MORTALITY OF DIABETIC CHILDREN—A REMEDIAL AND THEREFORE HOPEFUL INDEX OF THE FUTURE OF THE DIABETIC CHILD. E. P. JOSLIN, Ann. Int. Med. **11**:348 (Jan.) 1938.

Joslin discusses the needlessness of death from coma in diabetic children. He stresses the precautions to be taken during acute illness. He advises the organization of mobile coma units for areas without efficient laboratories and urges that every diabetic child be regarded as presenting a possibility of coma and friends, relatives and family doctor made to realize this thoroughly. Plans should be formed in advance for proper hospitalization of diabetic children.

In discussing needless death from tuberculosis, he states that the tuberculin test should be done early and frequently and that if it is positive the patient should be studied with the roentgen rays. These rules should apply increasingly as long as the patient lives.

Death from hypoglycemia usually results from mistaking hypoglycemia for coma.

Better results will follow more persistent individual educational effort for each child. READING, Galveston, Texas.

CREATINURIA AND CREATINE TOLERANCE IN CHILDHOOD. E. KOST SHELTON and B. N. TAGER, Endocrinology **21**:773 (Nov.) 1937.

In addition to the classic forms of hypothyroidism in children, classified as cretinism and childhood myxedema, the authors call attention to a third inadequately described form, which is four times more common than the others and is characterized by dwarfism and psychomotor retardation.

The only common factor in these three forms was osseous retardation. Determinations of the basal metabolism and serum cholesterol were diagnostically not particularly helpful.

In a search for further biochemical aids in diagnosis creatine metabolism was studied. Diminished basal creatinuria and an increased tolerance for ingested creatine as compared with the normal was found.

Children presenting a moderate degree of osseous retardation without clinical evidence of subthyroidism were found to have an increased basal creatinuria and no deviation from the normal in tolerance for ingested creatine.

JACOBSEN, Buffalo.

THE EFFECT OF SPLENECTOMY ON THE WEIGHT OF THE HYPOPHYSIS OF THE ALBINO RAT. LINDEN F. EDWARDS and CLARENCE W. WRIGHT, Endocrinology **21**:808 (Nov.) 1937.

Splenectomy was found to cause an increase in weight of the hypophysis of the rat.

JACOBSEN, Buffalo.

ALTERATIONS IN THE PERCENTAGE OF CELL TYPES IN THE HYPOPHYSIS BY GONAD TRANSPLANTATION IN THE RAT. CARROLL A. PFEIFFER, Endocrinology **21**: 812 (Nov.) 1937.

There is a definite pattern in the pituitary gland of the rat which is distinct for each sex. Each pattern is represented by characteristic percentages of cell types. Both the physiologic and the histologic characters may be altered within the limits of this pattern, but attempts to alter the pattern after the pituitary gland has become completely differentiated have thus far been unsuccessful.

JACOBSEN, Buffalo.

EFFECTS OF PARATHYROID EXTRACT AND OF VITAMIN D ON BLOOD PHOSPHATASE, CALCIUM AND PHOSPHORUS IN OSTEOGENESIS IMPERFECTA. A. E. HANSEN, I. MCQUARRIE and M. R. ZIEGLER, Endocrinology **22**:1 (Jan.) 1938.

It has been shown repeatedly that in osteogenesis imperfecta the calcium, inorganic phosphorus and proteins of the blood serum and the acid-base equilibrium are normal but that calcium and phosphorus are retained in subnormal amounts. No adequate explanation for this has been advanced.

The authors studied plasma phosphatase activity, calcium and phosphorus in 4 cases of this disease in which treatment was carried on with parathyroid extract and with large doses of viosterol. Both agents produced negative calcium and phosphorus balances and lowered phosphatase activity and are therefore contraindicated in this disorder.

JACOBSEN, Buffalo.

EXPERIMENTAL ACUTE HYPERPARATHYROIDISM. A. CANTAROW, H. L. STEWART and E. L. HOUSEL, Endocrinology **22**:13 (Jan.) 1938.

Acute hyperparathyroidism was induced in 6 adult dogs by injecting from 2,700 to 3,500 units of parathyroid extract over a period of seventy-two hours. Autopsies revealed degenerative changes and deposits of calcium in the areas which had undergone regressive changes. Fetuses in one of the experimental animals showed none of these changes, suggesting that the active parathyroid factor does not pass the placental barrier in significant amounts.

JACOBSEN, Buffalo.

USE OF ADRENAL CORTEX PREPARATIONS IN THE TREATMENT OF ASTHENIA. E. S. GORDON, E. L. SEVRINGHAUS and M. E. STARK, Endocrinology **22**:45 (Jan.) 1938.

A series of 32 cases of asthenia is presented, accompanied by the important clinical data. In 15 of these cases the condition was apparently due to factors

other than insufficiency of the adrenal cortex. In the remaining 17 prompt definite help was obtained by the administration of preparations of adrenal cortex. The blood pressure in these instances of adrenal asthenia paralleled the clinical status of the patient and the intensity of the therapy. There is a deficient mechanism for the storage of vitamin C in adrenal insufficiency.

JACOBSEN, Buffalo.

FURTHER OBSERVATIONS ON THE RELATION OF THE ADRENAL CORTEX TO EXPERIMENTAL DIABETES. F. D. W. LUKENS and F. C. DOHAN, Endocrinology **22**:51 (Jan.) 1938.

Experiments are described which show that an extract of adrenal cortex is capable of restoring to a considerable extent the diabetes of adrenalectomized-depancreatized animals. The factors suggested as favoring this response (species, salt intake, estrus, adrenal remnants) are noted.

An increase in urinary excretion of dextrose and nitrogen was observed in two hypophysectomized-depancreatized cats to which this extract had been given.

JACOBSEN, Buffalo.

RELATION OF THE THYROID GLAND TO THE SPONTANEOUS ACTIVITY OF THE RAT. V. E. HALL and M. LINDSAY, Endocrinology **22**:66 (Jan.) 1938.

In male rats thyroidectomy produced a fall in spontaneous running in rotating cages to about one-half the preoperative level, this fall being completed within the first three days after the operation. The positive correlation between activity and basal metabolism in animals not operated on persists after operation. Restoration of the normal resting metabolic rate by administration of dinitrophenol not only failed to restore normal activity but depressed the postthyroidectomy level still further.

The influence of the thyroid gland in maintaining normal activity of the type studied is therefore independent of its effect on the general metabolic rate.

JACOBSEN, Buffalo.

PITUITARY DWARFISM WITH DIABETES MELLITUS. H. G. BECK and G. M. SUTER, Endocrinology **22**:115 (Jan.) 1938.

The diabetogenic substance as well as the growth factor is believed to be elaborated in the eosinophilic cells of the anterior lobe of the pituitary. Hypophysectomy ameliorates experimental diabetes. Despite these observations pituitary dwarfism and diabetes mellitus coexisted in a 15 year old boy. Remarkable results were obtained with extract of anterior lobe containing gonadotropic and growth-promoting substances.

JACOBSEN, Buffalo.

CRETINOID EPIPHYSEAL DYSGENESIS. W. A. REILLY and F. S. SMYTH, J. Pediat. **11**:786 (Dec.) 1937.

Dysgenesis of the epiphyses occurred in 5 patients with severe hypothyroidism. The abnormally developing epiphyses have the following characteristics: There are multiple loci of calcification; the calcification is slow; in many parts of the skeleton the epiphyses are abnormal; the distribution usually is bilateral; the process occurs usually in the capital epiphyses, and there may never be normal structure without therapy. When thyroid extract is used, normal epiphyses develop in as short a time as from six to twelve months. Dysgenesis is frequently mistaken for the chondrodystrophy of Calvé-Legg-Perthes disease.

FROM AUTHORS' SUMMARY.

A New Syndrome Apparently Due to Over-Activity of the Posterior Pituitary. E. I. Jones, Lancet **1**:11 (Jan. 1) 1938.

A patient who was under observation for eight months had hypertension, hyperchromic anemia, achlorhydria and abnormal tolerance for carbohydrate, associated with urinary excretion of a substance which had the action of an extract of the posterior lobe of the pituitary gland. It is suggested that the syndrome was due to hyperfunction of the posterior lobe of the pituitary gland.

Langmann, New York.

Substances Controlling the Growth of Implanted Tumours. W. Moppett, M. J. Australia **2**:1065 (Dec. 18) 1937.

Moppett found that extracts of the anterior lobe of the pituitary, containing both growth-stimulative and gonadotropic substances, appeared to accelerate the growth of an implanted mouse tumor (S 37) and that thyroxin in certain circumstances retarded the growth of such a tumor.

Gonce, Madison, Wis.

Cretinism (Untreated) with Bone Changes Simulating Osteochondritis (Perthe's Disease of Hip). R. C. Jewesbury, Proc. Roy. Soc. Med. **31**:74 (Dec.) 1937.

A case is reported in a girl of 8½ years. The previous history, the family history and the results of physical examination and other investigations are given in detail in the report.

Williamson, New Orleans.

The Anterior Pituitary Lobe in Graves' Disease and in Myxoedema. C. L. Cope, Quart. J. Med. **7**:151 (Jan.) 1938.

Cope presents evidence which confirms the already accepted conclusion that the secretory activity of the thyroid gland is influenced by the anterior lobe of the pituitary gland through the mediation of a thyrotropic hormone: The hormone was shown to be present in the human pituitary gland and in the blood of thyroidectomized rabbits. Normal human serum did not possess thyrotropic activity when injected into young guinea pigs. Serum from patients with exophthalmic goiter exerted a depressing rather than stimulating effect on the thyroid glands of guinea pigs. The serum of 2 myxedematous persons showed no trace of thyrotropic activity. Concentrates of large volumes of normal urine and of urine from patients with exophthalmic goiter caused an increase in the weight of the thyroid gland in guinea pigs without hyperplasia.

Bradford, Rochester, N. Y.

A Case of Froehlich's Syndrome. A. Aguiar and J. C. Da Silveira, J. de pediat., Rio de Janeiro **4**:367 (Sept.) 1937.

An 11 year old boy presented the syndrome of adiposity and genital dystrophy, with undescended testes. Roentgenograms showed hypophysial enlargement. The authors gave the boy 100 units of a gonadotropic substance each day for ten months, as well as antisyphilitic therapy. The sella diminished in size, the testicles descended, and the boy lost 5 Kg. and became more active.

Sanford, Chicago.

A Case of the Waterhouse-Friderichsen Syndrome. H. Sulzer, Kinderärztl. Praxis **8**:508 (Dec.) 1937.

A typical case of the Waterhouse-Friderichsen syndrome is described, in which meningococci were found in the routine blood smear. Confirmation of adrenal hemorrhage was made by autopsy.

Heymann, Cleveland.

Diseases of the Muscles, Bones, Joints and Lymph Glands

HEREDITARY HYPOPLASIA OF THE MESENCHYME (BLUE SCLEROTICS AND BRITTLE BONES). G. E. BURCH and W. A. SODEMAN, Am. J. M. Sc. **194**:844 (Dec.) 1937.

Of 76 persons studied (one family tree), 53.9 per cent were found to be affected with hereditary hypoplasia of the mesenchyme. Seventeen were males; 24, females. All had blue scleras; 17 had had one or more fractures. A classification of idiopathic fragility of bone is given. The group described exemplifies the hereditary type.

HENSKE, Omaha.

PRESENT STATUS OF RHEUMATISM AND ARTHRITIS: REVIEW OF AMERICAN AND ENGLISH LITERATURE FOR 1936. P. S. HENCH and others, Ann. Int. Med. **11**:1089 (Jan.) 1938.

In this article of 135 pages the authors review 593 articles and 15 books. It is the "Fourth Rheumatic Review" prepared by the Editorial Committee of the American Rheumatism Association. Included in the review are gonococcic arthritis, tuberculous arthritis, syphilitic arthritis and synovitis, rheumatic fever in all of its phases, chronic arthritis, meningococcic arthritis, hemophilic arthritis and other forms of this disease.

READING, Galveston, Texas.

MESENTERIC LYMPHADENITIS AND THE ACUTE ABDOMEN. W. E. ADAMS and M. B. ONLEY, Ann. Surg. **107**:359 (March) 1938.

Inflammation of the mesenteric lymph nodes was recognized and discussed as early as the eighteenth century. The diagnosis was usually made after the patient came to autopsy. When the disease first became a definite clinical entity, it was thought to be in all cases tuberculous. This misconception was corrected when guinea pigs which had received injections of material from nodes removed at operation remained free from tuberculosis. The Mantoux test did much to differentiate the two types preoperatively. Although the appendix and small intestine have received the major consideration etiologically, it is not unlikely that the enlargement of the mesenteric lymph nodes is a local manifestation of a generalized condition having its origin in an infection of the upper part of the respiratory tract.

The colicky nature of the abdominal distress and the multiplicity of attacks of relatively short duration and frequent association with infections of the upper part of the respiratory tract are characteristics of the disease.

The disease is chiefly one of children.

Exploratory celiotomy is the treatment of choice, especially when a definite diagnosis cannot be made. The appendix is removed and the wound closed without drainage.

The prognosis for a permanent cure is good. Most of the patients remain symptom free following appendectomy. This is also the result in cases in which no operation is done if controlled medical management and antituberculosis measures are observed.

Twelve cases of nontuberculous and a single case of tuberculous mesenteric lymphadenitis are reported in this paper.

BANTIN, Omaha.

CONGENITAL DISLOCATION OF THE SHOULDER AND OTHER ANOMALIES. L. COZEN, Arch. Surg. **35**:957 (Nov.) 1937.

A case of dislocation of both shoulders from the time of birth is presented. It is not known whether the deformity was truly congenital in the sense of an intrauterine maldevelopment or whether it was incidental to trauma at birth. Other abnormalities were also noted in this case. The literature on this subject is thoroughly reviewed.

KAISER, Rochester, N. Y.

PROGRESSIVE MUSCULAR DYSTROPHY. L. BELINSON, Illinois M. J. **73**:206 (March) 1938.

Belinson reports 3 cases in which progressive muscular dystrophy was coincident with mental deficiency. Prostigmin was tried in a single case, with negative results.

BARBOUR, Peoria, Ill.

IMMUNOLOGICAL STUDIES IN CHRONIC STAPHYLOCOCCAL OSTEOMYELITIS. K. E. HITE, S. W. BANKS and G. M. DACK, J. Bact. **35**:53 (Jan.) 1938.

The tendency toward recurrence and the prolonged convalescence which frequently follows surgical treatment of chronic osteomyelitis have led the authors to investigate some of the host-parasite relationships in this disease. A study has been made of staphylococcic antihemolysin titers on the serum of patients with this disease. These tests have been repeated in the same cases over a period of several months. A marked correlation of the titer with the clinical condition of the patient has been manifest, the titer being elevated at times of acute exacerbation and reduced during periods of quiescence. Injections of toxoid given to patients in the chronic stages, while causing a rise in antihemolysin, failed to alter the course of the disease. Titers dropped rapidly after these injections were stopped. Since staphylococci causing osteomyelitis seem to be fair toxin producers, and since the antihemolysin content of the patient's serum has been shown to drop in the chronic stages of the infection and to be elevated by injections of toxoid without altering the course of the disease, it seems possible that some reaction of the host may be influencing antigen-antibody relationships in this chronic condition.

STOESSER, Minneapolis.

CHOLINE ESTERASE IN MYASTHENIA GRAVIS. A. B. CORKILL and A. H. ENNOR, M. J. Australia **2**:1121 (Dec. 25) 1937.

Two cases of myasthenia gravis studied by the authors failed to show any increase in the choline esterase activity of the blood. Both patients were temporarily relieved by administering prostigmin (the dimethylcarbamic ester of 3-hydroxyphenyltrimethylammonium methylsulfate, a derivative of physostigmine, which inhibits esterase activity). Despite this, however, the only safe assumption to be made in regard to myasthenia gravis is that there is either deficient production of acetylcholine at the neuromuscular junction or that esterase activity is locally increased.

GONCE, Madison Wis.

CLINICAL OBSERVATIONS ON CHAUFFARD-STILL DISEASE. N. A. ZUCKERMANN and E. J. K. MINSKY, Arch. de méd. d. enf. **40**:809 (Dec.) 1937.

Only 100 cases of this disease have been reported since its description in the years from 1896 to 1897. It is not yet certain whether the disorder represents an allergic reaction following repeated introduction of various nonspecific agents. There is no agreement at all concerning its relation to tuberculosis, especially the rheumatismal form described by Poncet. With respect to the causes, clinical evolution, pathogenesis and prognosis there is similar lack of accord.

The authors report 2 cases in infants, with the customary appearance of tumefaction of the knee joints, atrophy of the lower limbs and enlargement of the spleen and lymph glands. Tests for tuberculosis and syphilis were negative, and roentgenologic examination revealed no bony changes.

AMESSE, Denver.

SCAPHOCEPHALY AND SOME OBSERVATIONS ON STENOCEPHALY. J. PRATS and R. H. BEGNERIC, Cir. ortop. y traumatol., Habana **5**:102 (April-June) 1937.

The authors present a case of scaphocephaly and review stenocephaly in general. They give the differential diagnosis.

HERRON, Monroe, La.

CONGENITAL DISLOCATION OF THE HIP. A. INCLAN, Cir. ortop. y traumatol., Habana **5**:147 (July-Sept.) 1937.

Inclan opposes the idea of delaying the beginning of treatment till the age of 2 years. Early diagnosis and treatment of congenital dislocation of the hip are essential, as the bearing of weight aggravates the pathologic changes in the joint surface. Progressive abduction and internal rotation started in the first months of life can cure or decidedly favor the repair of congenital dislocation of the hip. Putte's apparatus is used.

HERRON, Monroe, La.

INCIDENCE OF CONGENITAL DISLOCATION OF THE HIP JOINT IN AUSTRIA. A. SONNENSCHEIN, Wien. klin. Wchnschr. **50**:1706 (Dec. 17) 1937.

It has been shown that congenital dislocation of the hip is frequent in certain regions and rare, if not nonexistent, in others. Sonnenschein reports a study of 786 cases from the records of the government orthopedic station in Austria between 1919 and 1933. Of the patients, 634 were born in Austria and 406 in Vienna. He notes that there was a high incidence in industrial centers but that the condition also occurred in less densely populated regions, as along the Czechoslovakian border. For example, at Nikolsburg, Czechoslovakia, 7 cases were reported in a population of 1,253.

Lange expressed the belief that the crossing of different racial characteristics is the cause of the luxation, and this might account for a greater occurrence along the borders of a country or in cosmopolitan centers. On the other hand, it would not account for the frequent occurrence of dislocation of the hip in such regions as upper Austria or in the Tyrol, where the population is homogeneous. Here, however, marriage between blood relations is more common than in communities with a mixed population, and the inbreeding of a recessive mendelian characteristic such as a tendency toward dislocation of the hip would undoubtedly cause a high incidence. It is possible, too, that such a recessive characteristic might become dominant in the next generation and account for cases in which there is a question of blood relationship of the parents.

[A similar preponderence of cases in certain provinces of northern Italy is reported by A. Poli, who also believes that intermarriage of relatives is responsible for this regional incidence. Abstracter.]

ABT, Chicago.

Skin Diseases; Allergy

AUTO PASSIVE TRANSFER IN ALLERGY. D. M. COWIE, Ann. Int. Med. **11**:949 (Dec.) 1937.

By "autopassive transfer" is meant the transfer of a patient's own passively sensitized serum into his own skin. Evidence is cited to show that the skin of an allergic person may fail to react to an intradermal injection of an allergen to which he is sensitive and yet react when a test is made at a site which has received an injection of his own serum.

The method of procedure and illustrative cases are given. The technic is not offered as a substitute for the Prausnitz-Küstner method of passive transfer.

READING, Galveston, Texas.

TRANSMISSION OF RAGWEED POLLEN ANTIGEN THROUGH THE BREAST MILK. A. STERLING and A. E. FISHMAN, Arch. Pediat. **55**:172 (March) 1938.

It is a safe procedure to treat pregnant women with a pollen extract, as normal children were born to mothers so treated. Allergic symptoms were observed in a 6 week old infant that was breast fed by its mother while she was receiving an extract of ragweed pollen. The symptoms regressed. It is concluded that pollen antigen is probably transmitted through the breast milk.

ORR, Buffalo.

STUDIES IN EXPERIMENTAL HYPERSENSITIVENESS IN THE RHESUS MONKEY: V. THE TECHNIQUE FOR DEMONSTRATING THE ABSORPTION OF UNDIGESTED PROTEIN. H. W. STRAUS and M. WALZER, J. Allergy **9**:121 (Jan.) 1938.

Serums from 3 persons suffering from asthma were used. They were shown to contain reagins for peanuts and cottonseed. In each experiment the skin of a monkey (Macacus rhesus) was sensitized with an intracutaneous injection of 0.05 cc. of the undiluted human serum. Between forty-eight and ninety-six hours after the injection of serum peanut milk or cottonseed milk was administered. The animal was deprived of food for twenty-four hours preceding the test meal.

Five tests were done on 4 animals. Positive cutaneous reactions developed at the sensitized sites after all five feedings. The absorption time when the feeding was given by gavage was from five to ten minutes. In an animal while anesthetized with pentobarbital sodium to which a third of a feeding was given the absorption time was twelve minutes.

The experiments confirm the finding that unaltered protein may enter the circulation from the gastrointestinal tract.

HOYER, Cincinnati.

ACQUIRED SPECIFIC HYPERSENSITIVITY TO SIMPLE CHEMICALS: I. ECZEMATOUS SENSITIVITY TO CLOTHING AND TO COSMETICS, WITH SPECIAL REFERENCE TO DYES. J. GOODMAN and M. SULZBERGER, J. Allergy **9**:136 (Jan.) 1938.

Allergic eczematous dermatitis was present in a large group of persons as a result of contact with dress materials, also in a few as a result of contact with shoes and as a result of the use of cosmetics. It is felt that the dyes used in the dress materials, shoes and cosmetics were responsible, and this could be proved in many instances by patch tests. While in all the cases reported the condition occurred in adults, it was brought out in discussion that contact dermatitis can and does occur in children and that cases have been reported in which the dermatitis resulted from contact with materials in zipper suits.

HOYER, Cincinnati.

GOLD CURVE OBTAINED WITH ALLERGIC BLOOD SERUM. J. M. ANDERSON, J. Allergy **9**:180 (Jan.) 1938.

A series of experiments were performed with colloidal gold solution, sodium chloride solution, normal blood serum and blood serum from an allergic patient. The colloidal gold curve obtained with serum from an allergic patient differed from that obtained with normal serum. The author infers from the character of the curve that allergic blood serum lacks some protein that is present in normal serum.

HOYER, Cincinnati.

RELATION OF INCIDENCE OF HUMAN AND ANIMAL SERUM DISEASE. M. J. FOX, J. Infect. Dis. **61**:341 (Nov.-Dec.) 1937.

The simple equation of $I = K\sqrt{C}$, in which I is the incidence, C the amount injected and K the constant for the particular serum, has been used to determine the incidence of serum sickness in a large series of serum-treated patients.

Comparison of the author's series of cases with those reported in the literature shows close similarity. The incidence of the reactions to human convalescent serum approaches a fixed minimal number of reactions of such negligible significance that it may be considered of no material consequence.

TOOMEY, Cleveland.

PROPHYLAXIS OF POISON IVY: USE OF AN ALMOND OIL EXTRACT IN CHILDREN. L. C. BACHMANN, J. Pediat. **12**:31 (Jan.) 1938.

Fourteen children ranging from 3 to 11 years of age, members of a large group institutionalized for various problems of behavior and for neurologic disturbances,

were selected for study because there were definite clinical records that they had had ivy poisoning or because they had extensive dermatitis due to this cause at the time of the experiment. The product used for prophylaxis and treatment of ivy poisoning was made up of approximately 0.66 per cent of a purified extract of poison ivy in almond oil containing about 5 per cent acetone. All injections were given into the gluteal muscle. At the time the first injection of 1 cc. was given, 6 children had clinical evidence of poisoning. Two weeks later a second injection was given, and only 3 children had evidence of the disease. On the sixteenth day following the injections, at a time when all the patients were free from any evidence of dermatitis, they were exposed to poison ivy. Two weeks later 7 of the children were given a third injection of the same material in a similar dosage.

Of the 14 children receiving two injections, as well as the 7 receiving three injections, none were noted to have gained any more protection than the untreated ones with whom they were associated. Three (50 per cent) of the 6 children with lesions at the time of the first injection presented new lesions within four days. All 3 of the children who had ivy poisoning at the time of the second injection presented new lesions within four days following the administration of the drug. All the children except a child who had lesions at the time of either the first or the second injection failed to show complete clearing up within ten days. Even though 14 patients received two injections of the extract of poison ivy, 12 (85.7 per cent) acquired new lesions after a deliberate exposure to the plant. Bachmann concludes that no significant prophylactic or therapeutic results were realized.

RAUH, Cincinnati.

SERUM REACTIONS AFTER INJECTION OF CONCENTRATED THERAPEUTIC SERUM. H. M. DAVIS, Lancet **1**:193 (Jan. 22) 1938.

An analysis is made of the incidence and manifestations of reactions occurring in a series of 4,835 patients treated with concentrated diphtheritic antitoxic serum. General reactions developed in 17.5 per cent, and if local reaction and albuminuria are included, in 21.9 per cent. Such reactions occurred with the greatest frequency in the first five years of life. Three main types of rash occurred: urticarial, erythematous and morbilliform.

LANGMANN, New York.

FAMILIAL ECTODERMAL DEFECT. R. T. BRAIN, Proc. Roy. Soc. Med. **31**:69 (Dec.) 1937.

A girl of 12 years showed pale straw-colored hair from 3 to 4 inches (7.5 to 10 cm.) in length, silky, fine and wavy. Microscopic examination of the hair showed absence of pigment. The lower incisors were round thin conical pegs, and the canines were similar. The molars were better shaped but small. The superior maxilla appeared somewhat underdeveloped. The nails showed slight dystrophy. The father also showed slight dystrophy of the nails. A brother aged 14 years suffered from dry skin and had only ten teeth in the upper jaw and had had eight in the lower, of which only five remained. They were peg shaped and widely separated.

WILLIAMSON, New Orleans.

ALOPECIA AREATA IN AN INFANT. C. M. WARREN, Proc. Roy. Soc. Med. **31**:84 (Dec.) 1937.

Alopecia areata was reported in a boy of 15 months. He had had for nine months two typical patches of it in the occipital region, where new growth of hair was already showing. The child's father, uncle, paternal grandmother and paternal grandaunt had all suffered from alopecia areata at some time of life. Alopecia areata occurring in three generations appears to be rare, although the hereditary influence is definitely recognized.

WILLIAMSON, New Orleans.

Teeth and Dentistry

NUTRITION AND DENTAL CARIES. B. R. EAST, Am. J. Pub. Health **28**:72 (Jan.) 1938.

East reviews the studies of three groups of authors on the influence of diet in bringing about arrest and inhibition of dental caries. His conclusions are: 1. Improving the diets of children living under controlled conditions seems to lessen the occurrence of caries. These results seem uninfluenced by the use of an antiseptic mouth wash. 2. The seasons seem to affect the appearance of caries —that period most remote from summer having the greatest incidence. 3. Vitamin D seems to play an important role in the occurrence of seasonal caries; its presence in the body either as a result of direct exposure of the skin to ultraviolet rays or through inclusion in the diet tends to lessen the seasonal variation. 4. A diet which inhibits caries without added vitamin D becomes more inhibiting when vitamin D is added either as cod liver oil or as vitamin D milk.

LIMPER, Louisville, Ky.

INFERIORITY COMPLEXES AND DENTAL ART. E. CHARRON, Union méd. du Canada **66**:414 (April) 1937.

In a brief article, Charron calls attention to the need of orthodontia to prevent feelings of inferiority in growing children.

DAFFINEE, Boston.

THE PREVENTION OF DENTAL CARIES DURING PREGNANCY AND LACTATION. A. BUCHER, München. med. Wchnschr. **84**:734 (May 7) 1937.

The vitamin C requirement during pregnancy is two to six times the normal. The marked deficiency of vitamin C is a factor in dental caries. Bucher gave 25 pregnant women large quantities of vitamin C. None of the patients had anemia after this treatment and there were fewer colds and fewer complaints of backache and fatigue. Vitamin C can be adequately supplied by means of a carefully selected diet or by the administration of ascorbic acid.

BRAHDY, Mount Vernon, N.Y.

AURAL SYMPTOMS DURING THE FIRST DENTITION. L. HOFMANN, München. med. Wchnschr. **84**:1407 (Sept. 3) 1937.

There is considerable difference of opinion as to whether dentition can produce fever, gastrointestinal disturbances or other symptoms. Hofmann has observed certain symptoms referable to the ear which are associated with the first dentition. The infant may rub or pull at the lobe of the ear or in other ways indicate that there is something irritating him in that region. Examination reveals that the external ear and the drum are normal but that the gums are usually red and swollen. The condition is considered to be otalgia nervosa.

BRAHDY, Mount Vernon, N. Y.

Miscellaneous

MECHANISM OF THE TOXIC EFFECTS FROM COMBINED USE OF CALCIUM AND DIGITALIS. J. S. GOLDEN and W. A. BROWN, Ann. Int. Med. **11**:1084 (Jan.) 1938.

In a series of experiments on dogs in which digitalis and calcium gluconate were given simultaneously and in another series in which the drugs were given thirty minutes apart, it was found that under the latter condition death occurred invariably and that when the drugs were given simultaneously marked toxic effects or death occurred in a majority of the instances. Death was associated with rapid

fall in blood pressure, ventricular tachycardia and ventricular fibrillation. The conclusion reached was that intravenous injection of calcium in a patient who is receiving digitalis is dangerous since the margin of safety is narrow and toxic effects can neither be foreseen nor successfully treated when they arise.

READING, Galveston, Texas.

TRANSFUSION OF BLOOD AND OTHER FLUIDS IN INFANCY. G. ORMISTON, Lancet **1**:82 (Jan. 8) 1938.

Ormiston recommends using the superficial temporal vein for the administration of fluids to infants by means of a hypodermic needle. The rate of inflow is limited so that there is no danger of pulmonary edema or of cardiac embarrassment from too rapid injections. However, the acquisition of the technic requires time, patience and a good deal of practice.

LANGMANN, New York.

SOME DANGER SIGNS IN CHILDHOOD. S. F. MCDONALD, M. J. Australia **2**:1107 (Dec. 25) 1937.

McDonald skips over the major danger signs and emphasizes some of the less obvious but none the less important symptoms seen in children.

The character of the cry is frequently of help when one can distinguish between them, the meningeal cry, for example, being quite characteristic, as is the whining, miserable cry in acrodynia. Also lack of expression is important and may suggest mental retardation. Delay in walking may indicate muscular dystrophy, cerebral defect or congenital dislocations. McDonald states that it is the physician's duty to warn the parents of a child with a muscular dystrophy that further children are liable to suffer from the same condition.

The facial expression alone enables one to recognize mongolism, marasmus and syphilis and is quite suggestive in the case of scurvy and in that of rickets. The expression is also characteristic in acrodynia and such acute illnesses as pneumonia. The expression in acute nephritis is likewise suggestive. Pain is usually a reliable symptom in children, but every pain in childhood should not be assigned to the teeth or to the gastrointestinal tract, but a thorough search should be made for conditions varying from tumor of the brain and lead poisoning to osteomyelitis.

Laryngeal obstruction is always a danger sign requiring close attention.

TENNEY, Madison, Wis.

SHOCK FOLLOWING TRANSFUSION. S. TASSOVATZ and B. TASSOVATZ, Arch. de méd. d. enf. **40**:803 (Dec.) 1937.

Transfusion during the course of an acute infectious disease, pernicious anemia or leukemia is followed almost invariably by shock of variable intensity. Occasionally one may find a latent response, with leukopenia or slight fever, but most common is acute shock with oscillation of temperature and chilly sensations, often accompanied by vomiting, more or less nervous agitation, pallor and rapid pulse. This is designated by Jeanbreau as a posttransfusional reaction.

In certain cases, especially during the progress of an infection, the reaction is much more severe; here one notes symptoms appearing in ten or twenty minutes (anaphylactic phenomena) or within several hours (group incompatibility).

Whether benign or grave, transfusional shock presents all the characteristics of colloidoclassic shock, as demonstrated by Joltrain and others. The pathogenesis of shock is still a matter for discussion. It is obvious that the problem is complex and that the reaction is not traceable in all cases to a single cause. Certain hypotheses appear to explain the majority of cases: According to Tzanick, the accidents following transfusion are attributable as much to the plasma as to the cells. There may be congenital intolerance among allergic subjects. In other instances the disease itself, through changes in the blood, may provoke shock.

The authors feel that too rapid transfusion is a factor and that citrated blood is apt to produce unfavorable reactions through colloidal changes. They conclude with the opinion that shock is probably most often produced by incompatibility between the plasma of the donor and the plasma of the patient.

AMESSE, Denver.

USE AND DOSAGE OF MORPHINE AND COUGH MEDICAMENTS IN CHILDHOOD. H. ZISCHINSKY, München. med. Wchnschr. **84**:1482 (Sept. 17) 1937.

The dosages of many drugs prescribed for children cannot be calculated from the adult dosages according to a set formula. Some drugs are well tolerated by children, and the dosage must be comparatively high before the desired therapeutic effect is attained. For allaying cough the following dosage of codeine in milligrams is recommended: in the first half year 0.003, in the second half year 0.005, for small children 0.01 and for children of school age from 0.02 to 0.03. If the desired results are not obtained, the dose should be increased. In addition to some proprietary products, Zischinsky also discusses the use of morphine. There are certain limited but definite indications for the administration of morphine in the practice of pediatrics. The following dosage in milligrams is suggested: at 5 or 6 months of age 0.3 to 0.4, during the second half of the first year 0.4 to 0.5, for the second year 0.75 and for the third year 1. The dose may be increased gradually if necessary.

BRAHDY, Mount Vernon, N. Y.

THE DRINKING FOETUS: A ROENTGENOLOGIC STUDY. K. EHRHARDT, München. med. Wchnschr. **84**:1699 (Oct. 22) 1937.

Several years ago Ehrhardt described the visualization of an animal's placenta by an intravenous injection of thorium dioxide. The present communication deals with the question of whether the human fetus swallows amniotic fluid. De Snov injected saccharin solution and methylene blue into the amniotic fluid and then demonstrated them in the mother's urine.

Ehrhardt reports some interesting observations in a 21 year old woman during the sixth month of her pregnancy. The pregnancy was to be interrupted because of congenital feeblemindedness. Fifteen hours before the interruption 8 cc. of colloidal thorium dioxide was injected into the amniotic fluid. The injection was made under local anesthesia through the abdominal wall, midway between the symphysis and the umbilicus. Fifteen hours later an abdominal incision was made for removal of the fetus. The fetus was alive, and its movements were observed for several minutes. One roentgenogram was taken before the membranes were incised, another after incision and a third of the fetal intestine. (Photographs accompany the article.) All the thorium dioxide was in the gastrointestinal tract of the fetus. Apparently the fetus had swallowed and excreted all of the amniotic fluid, but the thorium dioxide was retained in the intestine.

BRAHDY, Mount Vernon, N. Y.

TREATMENT WITH SULFANILAMIDE. G. TÖRÖK, Orvosi hetil. **81**:1264 (Dec. 11) 1937.

It is well known that since Discombe called attention to the matter cyanosis and sulfhemoglobinemia have been often observed during treatment with sulfanilamide. Levy observed, besides, a diminution in the number of the red cells and in the hemoglobin content and furthermore an increase in the number of the reticulocytes. Levy thinks that sulfanilamide may be noxious for the marrow of the bones. Török examined the blood of infants and children, but he could not find any changes besides the moderate increase in the number of the reticulocytes, so that he recommends the use of sulfanilamide. Simultaneously with giving doses of this drug Török tried giving various doses of magnesium sulfate and examined the blood with a spectroscope but could not find either sulfhemoglobinemia or methemoglobinemia.

GÖTTCHE, Budapest, Hungary.

Society Transactions

CANADIAN SOCIETY FOR THE STUDY OF DISEASES OF CHILDREN

ALTON GOLDBLOOM, M.D., *President*

Sixteenth Annual Meeting, Kingston, Ontario, June 3-4, 1938

PEARL SUMMERFELDT, M.D., *Secretary-Treasurer*

First Session

Friday Morning, June 3

PRESIDENTIAL ADDRESS: STATUS OF PEDIATRICS. DR. ALTON GOLDBLOOM, Montreal.

CONTAMINATION AND STERILIZATION OF AIR. DR. ELIZABETH CHANT ROBERTSON, Toronto.

The effect of air conditioning and/or ultraviolet irradiation on the number of bacteria in the air of an operating room during use was determined. Ordinarily there were about 62 bacteria per cubic foot (28,317 cc.) of air; with air conditioning this number was reduced to 27; with ultraviolet irradiation, to 16, and with both air conditioning and ultraviolet irradiation to 6. The Wells air centrifuge and a simple absorbent cotton filter were used in making the counts. The organisms were due to the presence of people in the room. About 50 per cent of the bacteria were large cocci (commonly found in air); 25 per cent were staphylococci, and the remaining 25 per cent were mostly diphtheroids and aerobic spore bearers. Streptococci were rarely found.

Similar counts were found in cubicles containing 3 to 5 babies in the infants' ward. Much larger numbers of bacteria were found in the air of the crowded outpatient department and of large wards for older children.

The possibility of using air conditioning and ultraviolet irradiation to reduce air-borne infections in the wards is being investigated.

DISCUSSION

DR. E. A. MORGAN, Toronto: I still find it difficult to understand why the counts in the infants' ward were so low, because the number of persons per cubic foot of air is higher than in the other wards.

DR. ELIZABETH C. ROBERTSON, Toronto: In the older children's ward the cleaner puts specially prepared sawdust on the floor and then uses a mop, but in the infants' ward the floor is washed. That may be the reason for the difference between the numbers of bacteria in these wards. Also there is more movement in the medical ward than in the operating room or in the infants' ward.

DR. ALAN BROWN, Toronto: I think the use of masks in the infants' ward reduces the number of bacteria in the air there.

BILATERAL LOBECTOMY FOR BRONCHIECTASIS. DR. DUDLEY E. ROSS, Montreal.

(A short review of the literature was given, together with mortality rates, and the chief factors concerned with minimizing the dangers in the operation were discussed. In addition, 2 cases of successful bilateral lobectomy for bronchiectasis were reported with histories.)

DISCUSSION

DR. ALAN BROWN, Toronto: My associates and I have had a total of 14 cases in which lobectomy was done in a series of 115 cases of bronchiectasis. There were 3 deaths, 2 in cases in which the lobectomy was bilateral. One patient died from hemorrhage and the other 2 from aspiration of purulent material. What technic avoids death of patients treated by bilateral lobectomy, and what procedures are considered especially important in this operation? I doubt if we could agree with the statement that one should treat the patient early, before bronchiectasis has fully developed.

DR. DUDLEY E. ROSS, Montreal: I suppose Dr. Brown is talking about deaths which occur shortly after the operation, not immediately on the operating table. Inhalation anesthesia is the important factor in such deaths. In addition, I have found that when inhalation anesthesia is used the patient is apt to cough a good deal, and the purulent material may get into one of the lobes. With spinal anesthesia one does not have as much difficulty with this or as much struggling by the patient. I believe that the Toronto procedure has been a one stage operation in all cases, and I think this is an important difference. The mere fact of producing adhesions and immobilizing the lung on the side concerned must be of value to the patient in aiding him to withstand the effects of the operation. Many people attach a great deal of importance to the production of adhesions. Anything that will help lower the mortality is worth trying.

SHORT HISTORY OF THE INFANTS' HOME AND INFIRMARY OF TORONTO. DR. DORIS MONEYPENNY, Toronto.

The Infants' Home and Infirmary of Toronto is an agency caring for dependent and semidependent children under 4 years of age. Founded in 1875, this was the first institution in this city to admit children under 2 years of age. It was the pioneer in Canada in placing children in foster homes. The mortality rate per total population of the Infants' Home was reduced by this means from as high as 55 per cent to a level of 1 per cent or less. The number of foundlings has been reduced to a minimum by work with unmarried mothers.

DISCUSSION

DR. T. G. H. DRAKE, Toronto: Has any comparison been made of the cost per patient in the early days and now?

DR. E. CHANT ROBERTSON, Toronto: Was there an epidemic in the year in which high mortality occurred, and did this have some influence on the decision to have foster homes?

DR. DORIS MONEYPENNY, Toronto: In 1875 the total expenditure was less than $12 per person per year, but there were a great many donations of food, etc. In 1937 the per capita cost was $1.02 per day, which covered everything. In 1919 there were four epidemics, and this undoubtedly had a great deal to do with the decision to change the system to one of foster homes.

PERCUTANEOUS TUBERCULIN REACTION. DR. H. P. WRIGHT, DR. A. F. CHAISSON (by invitation) and MISS R. ALLISON (by invitation), Montreal.

An ointment somewhat similar to Hamburger's "percutan" was prepared by mixing old tuberculin, fuller's earth and hydrous wool fat. It contained approximately 40 per cent of tuberculin. A similar ointment lacking the old tuberculin was used as a control. After the skin was cleansed with ether, the ointment was rubbed on an area the size of a 50 cent piece with 60 revolutions of the finger.

Results obtained with this ointment in a small series of carefully studied cases have been consistently satisfactory. The cheapness and stability of the ointment warrant more extensive application of the test by physicians and nurses interested in detecting early stages of tuberculosis in children.

In our hands the percutaneous test has been as reliable as the intradermal injection of 0.1 mg. (0.1 cc. of a 1 : 1,000 solution) of old tuberculin. It is suggested not that this ointment should take the place of the various dilutions of old tuberculin or of the purified protein derivative used in hospital practice but that as a case finder outside hospitals it should enable physicians to discover many more cases of tuberculosis in children.

DISCUSSION

Dr. D. P. Arnold, Buffalo, N. Y.: Have Dr. Wright and his associates had any experience with the patch test?

Dr. Alan Ross, Montreal: How many cases were there in the first series?

Dr. H. S. Mitchell, Montreal: Do the patients ever have severe subjective symptoms?

Dr. H. P. Wright, Montreal: I think that the percutaneous test is simpler to perform and more economical than the patch test. The adhesive tape necessary in the patch test is hard to get off without irritation. However, I would not say anything against the patch test, and there is not much to choose between the two. We tested 44 patients in the tuberculosis wards and 57 in the general medical wards.

There were no subjective symptoms in our series. In some cases there was local irritation but no elevation of temperature.

Utilization of Calcium. Dr. Frederick F. Tisdall and Dr. T. G. H. Drake, Toronto.

Studies were made of the retention in the rat's body of calcium fed in various forms.

When to a diet low in calcium but otherwise normal, which included cod liver oil, calcium was added in the form of calcium carbonate, calcium chloride, dicalcium phosphate ($CaHPO_4$), calcium gluconate, calcium lactate, whole milk powder, casec or pablum, the percentage of the added calcium retained was essentially the same in each instance.

With a diet normal in phosphorus and low in calcium, the retention of phosphorus and calcium increased approximately in the ratio of 1 to 2 when retention of extra calcium was brought about by the addition of calcium to the diet. In other words, with a diet adequate in phosphorus the amount of phosphorus retained was dependent on the amount of calcium retained.

The addition of calcium in the form of large amounts of spinach to a diet low in calcium resulted in a reduction rather than an increase in the body calcium. This effect was probably due in part to the oxalic acid content of the spinach.

The increase in the body calcium produced by the addition of different cereals has been studied.

The inadequacy of an average human diet low in milk as a source of calcium was biologically demonstrated. Not only was the calcium content of this diet low, but the percentage of the calcium retained was less than when the same diet was given with added milk.

DISCUSSION

Dr. S. Graham Ross, Montreal: I was surprised to hear how well calcium chloride was retained. Calcium chloride is an acid-producing substance, and as such one might expect it to be a decalcifying agent. Possibly the amount used was not sufficient to produce that acid effect.

Dr. Frederick F. Tisdall, Toronto: Only a small amount of calcium chloride (200 mg. calcium per hundred grams of food) was added, and this was probably not sufficient to exert an acidifying effect.

SULFANILAMIDE THERAPY IN INFECTIONS. DR. NELLES SILVERTHORNE and DR. ALAN BROWN, Toronto.

A study was made of the use of sulfanilamide in the treatment of various infections in children, especially streptococcic meningitis. Our experience indicated that sulfanilamide is of value in the treatment of streptococcic infections of the skin and of gonorrhea.

DISCUSSION

DR. D. P. ARNOLD, Buffalo, N. Y.: What was the dose?

DR. S. GRAHAM ROSS, Montreal: What method of administration was used?

DR. T. G. H. DRAKE, Toronto: Were there reactions?

DR. D. P. ARNOLD, Buffalo, N. Y.: It has lately been thought that such a high concentration in the blood is not necessary. What is Dr. Silverthorne's opinion about this?

DR. NELLES SILVERTHORNE, Toronto: The dose varies with the individual patient but always has been over 15 grains (0.97 Gm.) per 20 pounds (9.1 Kg.) of body weight. A 5 year old child would probably receive 60 grains (3.88 Gm.) the first day. Sometimes the dose is later reduced. In the past few months the drug has been given by oral administration in tablet form. It is given every four hours, accompanied by the same amount of sodium bicarbonate. We have not seen any definite immediate reactions. The skin of the patients often becomes rather bluish gray while the drug is being used. There is often a rash four to ten days after the use of sulfanilamide or even during its administration. It looks like the rash of German measles. There was no definite decrease in the white blood cell count, certainly no decrease to injurious levels. Regarding the question of concentration in the blood, I think the work of C. C. Lucas is important. He has shown that one can keep the level in the blood only at a certain height, no matter how much one gives. On the other hand, Dr. Perrin Long, of Baltimore, stated that most physicians were not giving large enough doses. I believe that our doses are sufficiently large.

MANDELIC ACID VERSUS SULFANILAMIDE THERAPY FOR PYURIA. DR. PEARL SUMMERFELDT, Toronto.

Fifty-two patients with pyuria were treated either with sodium mandelate and ammonium chloride or with ammonium mandelate. Of these, 91 per cent had urine free of pus and bacteria in one to thirty-four days, the majority within one week; in 9 per cent there was no response to the drug. Failures in treatment were due to intolerance to the drug and to the presence of secondary chronic interstitial nephritis.

Twenty patients were followed for one to twenty-four months. Of these, 50 per cent had sterile urine from nine months to two years; 30 per cent had recurrence of their bacilluria in one to thirteen months, and 20 per cent had recurrence of their pyuria in thirteen to nineteen months. The recurrence of pyuria generally took place in cases of persistent involvement.

Forty patients with pyuria were treated with sulfanilamide and sodium bicarbonate. Of these, 75 per cent responded to treatment in one to thirty days, the majority within one week. In 15 per cent there was recurrence of the bacilluria as soon as the drug was discontinued, and in 10 per cent there was no response to treatment. These were all under the age of 2 years. Failure in treatment was due to cyanosis in 1 case and was undetermined in the others.

Eighteen patients were followed from three weeks to six months. In 66 per cent the urine was sterile for three weeks to six months. Bacilluria recurred in 11 per cent, and pyuria recurred in 23 per cent, in from one to three months.

It was hard to determine the relative value of each drug, but it is of interest that in 50 per cent of the patients with persistent pyuria treated with sulfanilamide

there was recurrence of the pyuria in one to three months, while among those treated with mandelic acid only 25 per cent had recurrence of their pyuria in thirteen to nineteen months.

DISCUSSION

DR. D. P. ARNOLD, Buffalo, N. Y.: Did Dr. Summerfeldt change from one drug to another in any cases of persistent pyuria? Are some infections better treated with sulfanilamide and others with mandelic acid?

DR. ALAN ROSS, Montreal: Is there any difference between the drugs used in cases of congenital anomalies?

DR. S. GRAHAM ROSS, Montreal: Was the water intake varied to see whether this caused variations in the concentration of the drugs in the urine? Did this alter the effect of the drug?

DR. PEARL SUMMERFELDT, Toronto: With regard to congenital abnormalities, there was no difference between the effects of the two drugs. I think mandelic acid is the better of the two. We did not try the effect of varying the water intake.

Second Session

Saturday Morning, June 4

RHEUMATIC INFECTION IN CHILDHOOD: EFFECT OF SURGICAL OPERATIONS ON THE BLOOD SEDIMENTATION RATE. DR. R. R. STRUTHERS and DR. H. L. BACAL, Montreal.

There is danger in the premature surgical treatment of foci of infection, such as the tonsils and adenoids, the paranasal sinuses and the teeth, in children suffering from the various manifestations of rheumatic fever. Surgical intervention should not be attempted until all evidence of activity of the rheumatic infection has been absent for a minimum of six weeks.

According to our experience, determination of the sedimentation rate is the most delicate test that can be used to determine the activity of the rheumatic infection. This test reacts in a characterisic way in cases of acute rheumatic fever, chorea and carditis, respectively.

Fifty nonrheumatic children, used as controls, and 100 children suffering from rheumatic fever and its various manifestations were compared as to the effect of surgical operations to eradicate foci of infection on the blood sedimentation rate. There were three types of reactions in both:

1. Some children showed no alteration in the sedimentation rate, with little or no loss of weight after operation.

2. Some showed a sharp rise and a sharp fall of the sedimentation rate, with an average loss in weight of 2 pounds (0.9 Kg.) in the controls and 4 pounds (1.8 Kg.) in the rheumatic children.

3. Some children showed elevation of the sedimentation rate before operation (probably due to the focus of infection and not due to the rheumatic infection) and a sudden and sharp drop to normal after operation.

In conclusion, children suffering from acute rheumatic fever and its manifestations are definitely more serious surgical risks than the normal child. They suffer more frequent postoperative complications, require a longer convalescence and lose an average of 4 pounds in weight, particularly after the removal of tonsils and adenoids.

RELATION OF CHOREA TO RHEUMATIC FEVER AND HEART DISEASE. DR. S. J. USHER, Montreal.

One hundred and five cases of chorea were observed for three years in a special rheumatic pavilion and in the outdoor cardiac clinic of the Children's Memorial Hospital. Fifty-six were cases of pure chorea and 49 of mixed chorea,

associated with other rheumatic manifestations. In 14 per cent of the cases of pure chorea and in 65 per cent of the cases of mixed chorea the condition was associated with heart disease. Removal of the foci of infection had no effect on the course of the chorea. It was felt that greater stress should be laid on the psychic element of chorea, as regards both treatment and prevention of recurrences.

DISCUSSION

Dr. Maude E. Abbott, Montreal: I was much interested in this paper. Of course I know well Osler's specimens in the McGill Medical Museum, which constituted the basis of his book on chorea and choreiform disorders. There are at least 3 of these in this museum at the present time. The rest of his study was done at the Infirmary for Nervous Diseases in Philadelphia. He followed his cases carefully, and the 3 specimens just mentioned were hearts showing severe endocarditis of patients who had had pure chorea without any rheumatic history. Dr. Burr, of Philadelphia, stated that perhaps the reason so little stress is laid on the incidence of endocarditis in cases of pure chorea at the present time is that much diagnostic work is now done with the fluoroscope and electrocardiogram and less attention is paid to the physical signs of valvular heart disease, so that a soft organic murmur originating in the course of chorea may sometimes escape detection.

Dr. A. P. Hart, Toronto: Was the chorea in these cases of the severe type?

Dr. S. J. Usher, Montreal: I found that in the majority of cases in which definite heart disease occurred the chorea was complicated with a rheumatic infection. In most of our cases involvement was mild. Few instances of severe type were seen. The degree of cardiac involvement was comparatively slight. Mitral stenosis was also slight.

Changes in the PR Interval of the Electrocardiogram in Rheumatic Fever. Dr. Leonard G. Parsons, Birmingham, England, and Dr. J. D. Keith (by invitation), Toronto.

The intensity of the first cardiac sound at the apex is related to the PR interval of the electrocardiogram. There is also a relation between the auricular and ventricular pressure curves and the changing intensity of the first cardiac sound. It was found that if the PR interval in children is 0.16 second or less, the first cardiac sound is almost always well heard. If it is 0.18 second, the first sound is diminished in intensity. If it is 0.2 second, the first sound is faint or inaudible. The frequency of the lengthening of the PR interval in cases of rheumatic fever was demonstrated from several aspects; it is suggested that changes in the conduction time of 0.04 second or more should be considered of importance, even when the greatest figure does not exceed 0.2 second. A number of children with prolonged PR intervals were given atropine, and a shortening of the conduction time was found to occur. This was accompanied by an increase in the intensity of the first sound. A murmur under these circumstances was sometimes found to obscure the first sound, making it difficult to pick out, but it seems unlikely that the murmur replaces the sound. For this reason it is suggested that the term "obscure" or "mask" is better than "replace" when one is referring to the relation of cardiac murmurs to sounds.

Various factors intensify or diminish the first cardiac sound.

DISCUSSION

Dr. S. J. Usher, Montreal: I understood Dr. Keith to say that the diagnosis of carditis was made on the presence or absence of a systolic murmur. My associates and I found systolic murmurs extremely variable in our cases of rheumatic fever.

Dr. Nelles Silverthorne, Toronto: Does not the speeding up of the heart rate due to the atropine decrease the PR interval?

Dr. R. R. Struthers, Montreal: Would Dr. Keith go so far as to say that an increase in the PR interval of 0.02 second is enough to justify a diagnosis of heart disease?

Dr. J. D. Keith, Toronto: An increase of 0.02 second might not be enough to justify this diagnosis. I think a marked lengthening is indicative of rheumatic fever. If there is a lengthening of 0.04 second or more there is almost certainly heart disease.

Dr. R. R. Struthers, Montreal: In the group of 200 cases just discussed, only 12 patients had acute rheumatic arthritis and escaped cardiac damage. Certainly in 200 of the cases observed by my associates and me there was nothing like that severe degree of damage. Only 6 per cent of the patients in the former group escaped it.

Dr. J. D. Keith, Toronto: I think we differ on what we consider arthritis. A high percentage of patients with vague pains in the joints do not have heart disease, but most children with definite acute rheumatic arthritis do have carditis.

The reason I chose the systolic murmur to differentiate these cases was that I thought it best to make the differentiation as simple as possible. The object in mind was to investigate the lengthening of the PR interval in patients with and without heart disease. Since the diagnosis of heart disease rests essentially on the systolic murmur, it was not thought necessary to go into the diagnosis any more accurately in order to bring out the point in mind. The marked shortening in the PR interval in the rheumatic patients given atropine was not due to the acceleration of the heart rate. The normal controls had only a slight decrease in the PR interval, whereas the rheumatic children had a marked diminution of conduction time with the same increase in the heart rate.

Studies on Vitamin C in the Blood During Pregnancy, Birth and Early Infancy. Dr. S. H. Jackson (by invitation) and Dr. Charles E. Snelling, Toronto.

The method used for determining the ascorbic acid content of the blood was examined, and several sources of error were discovered. To eliminate or control these errors, modifications were made in the method of analysis. With this modified procedure, we have measured the ascorbic acid content of the plasma of pregnant women. Toward the end of pregnancy there seems to be a slight fall. Factors incident to labor lower the ascorbic acid level in the maternal blood. The fetus acts as a parasite and has higher levels than maternal blood taken ante partum. Babies fed totally by breast from birth to the age of 5 months are receiving good vitamin C nutrition if the ascorbic acid content of the milk is greater than 4 mg. per hundred cubic centimeters; if the ascorbic acid content is below 2 mg. per hundred cubic centimeters in the breast milk, there is likelihood of a lack in the baby. In artificially fed babies of the same age group not receiving additional vitamin C, the level of ascorbic acid in the blood is low.

As a result of these studies, the following recommendations are made: Artificially fed babies should receive additional vitamin C from the age of 2 weeks. The mothers of breast-fed babies should have adequate vitamin C in the diet, and if there is any question of lack in the mother's diet, the baby should receive additional vitamin C.

DISCUSSION

Dr. Alan Brown, Toronto: This report has an important practical bearing: All physicians who see babies in the public wards of hospitals know how susceptible they are to intercurrent infections. This partial lack of vitamin C may be one of the reasons for their great lack of resistance.

FOCAL EPILEPTOGENIC LESIONS OF BIRTH AND INFANCY AND THEIR EVENTUAL RADICAL TREATMENT. DR. H. M. KEITH and DR. WILDER PENFIELD (by invitation), Montreal.

During the past few years, a considerable number of patients with focal epilepsy have been studied clinically and at operation. A number of these patients gave a definite history of injury at birth. Clinical evidence that such injury had occurred was also present. We have attempted to determine from the lesions observed at operation the type of injury to the nervous system which occurred at birth. The results of radical surgical treatment were also ascertained.

DISCUSSION

DR. ALAN BROWN, Toronto: Does Dr. Keith believe that in probably all cases epilepsy is due to injury at birth? Would he consider, or has he tried, the intravenous use of heparin in cases in which an early diagnosis of thrombosis has been made? My associates and I used heparin in 2 cases, in both of which postmortem examination was made. There seemed to be no ill effect from the use of this drug. In 1 case, in which it was used for ten days continuously, the clotting time reached seventeen minutes.

DR. C. E. SNELLING, Toronto: Dr. Keith shows scars which were removed, but I should imagine a new scar would be formed. How, then, did he get a good result?

DR. E. A. MORGAN, Toronto: Why is it that these children who were injured at birth showed no evidence of the injury for fourteen or fifteen years, although it must have been there all the time?

DR. H. M. KEITH, Montreal: We do not feel that all epilepsy is due to injury at birth. I have not used heparin at all. I think one should make an effort to use something of this kind in the cases of thrombosis. I have not had an opportunity of seeing enough of these patients at birth, but one sees them later, in the neurologic institutions. With regard to the mental state, 1 or 2 patients could not carry on without help. Some were in a better condition than others. The endeavor was to stop the attacks and give the patients relief. Dr. Snelling asked what condition is left in the brain. If a laceration, a hemorrhage or an injury to brain tissue is not clearcut, it leaves a scar. If the area is removed cleanly, it leaves only a space filled with fluid. It is surprising what little difference this makes in the patient's mental capacities. We have been studying the effects of removing frontal lobes, and the results make us wonder why one has a frontal lobe at all. Dr. Morgan asked me why the evidence of injury is seen only late. I think it is perhaps due to the fact that an area is damaged which does not give obvious signs. Sometimes one does not see the patients until a good many years after the injury. If there is a definite history of injury at birth it is generally found that the patient had some difficulty during the first twenty-four hours of life.

INTRODUCTION TO ELECTROENCEPHALOGRAPHY. DR. WILLIAM A. HAWKE (by invitation), Toronto.

In 1875 the electrical activity of the brain was first discovered. In 1924 Berger took the first records from the intact scalp of man. Since then a great deal of investigation has been carried on.

The apparatus required to record these currents consists of leads applied to the scalp, a powerful amplifier and means of recording either by light on films or by ink on paper.

The records obtained consist of A, B, C and D waves, plus periods of electrical inactivity and artefacts. The waves are distinguished by their frequency, their voltage, the areas from which they appear and the conditions which abolish them.

These waves probably arise from the cells of the cortex, the rate being an inherent property of the cells. The rate can be controlled, however, by other parts of the nervous system.

The waves show definite physiologic changes during sleep, anesthesia, anoxemia and hypoventilation, and they are different in infancy, in childhood and in adult life.

Variations due to disease are associated with dementias, tumors, convulsive states and many conditions of cortical damage. The most valuable applications of this method are the localizing of cortical tumors and the study of epileptic states.

DISCUSSION

DR. E. A. MORGAN, Toronto: Have these waves ever been found in a case in which there were cerebral scarring and epilepsy? Might it be possible that would answer my question to Dr. Keith? Are the electrical discharges the cause of the seizures?

DR. WILLIAM A. HAWKE, Toronto: With regard to Dr. Morgan's first question, cases have been reported in which there was a history of injury at birth and in which one could outline a scar by this technic. In these cases there is a great possibility of finding slow waves from the scar. Some people think the cause of these convulsions is a change in rhythm: The rhythm slows down in the cortical cells, and an attack of petit mal is produced. Now one can see what is going on inside the brain when a child is having convulsions. These electrical waves are a definite part of the convulsions and produce the clinical sign; but what produces the waves has not been settled with any finality.

DR. E. A. MORGAN, Toronto: They do not initiate convulsions?

DR. WILLIAM A. HAWKE, Toronto: They come before the convulsion, but something produces the electrical waves first.

DR. J. D. M. GRIFFIN, Toronto: Why does Dr. Hawke think these electrical waves arise in the cortex?

DR. WILLIAM A. HAWKE, Toronto: I think so because normal waves are obtained from areas of cortex which have been isolated except for their blood supply. Gradual excision of the various cortical layers by removal or coagulation would gradually wipe out certain of the waves. When all the cortex is destroyed, no waves are present.

DR. S. J. USHER, Montreal: What is the difference between the records obtained from normal and from hypertonic infants?

DR. WILLIAM A. HAWKE, Toronto: The artefacts obtained when one attempts to record waves of infants are so great that one cannot interpret with assurance the records obtained. Part of them may represent true cortical potentials, but a great many represent merely artefacts.

DR. D. P. ARNOLD, Buffalo, N. Y.: How does one obtain records of convulsions when the patient moves so much?

DR. WILLIAM A. HAWKE, Toronto: The potential from the convulsive disturbance is so large that it overrides the artefacts caused by movements.

GASTROINTESTINAL DISTURBANCES IN CHILDREN RESULTING FROM PSYCHOLOGIC FACTORS. DR. J. D. M. GRIFFIN (by invitation), Toronto.

In any children's clinic will be found many cases in which symptoms referable to the gastrointestinal tract occur without any demonstrable organic disease or defect. The common types of these functional symptoms include anorexia, regurgitation and rumination, persistent nausea and vomiting, constipation and diarrhea, involuntary defecation and epigastric and abdominal pains.

The summaries of 4 case histories illustrate these symptoms. On analysis the factors responsible for the symptoms can be classified as (*a*) endogenous (psycho-

logic), including obscure physical factors and factors relating to the intellectual and emotional make-up of the child, and (*b*) exogenous (environmental), including factors relating to the home and neighborhood, the family and playmates, the school and teacher and the recreational and social activities and facilities.

The treatment should be directed toward those factors which are most glaringly at fault and which are most easily corrected. The relation between the child and the physician, which is often overlooked, is extremely important. In the clinic for psychologic medicine at the Hospital for Sick Children, Toronto, about two thirds of the children with this type of symptom have become free from symptoms within six months of starting treatment. The remainder present special difficulties, which require special supervision or drastic treatment.

DISCUSSION

DR. A. M. DOYLE, Kingston, Ontario: Has Dr. Griffin any figures concerning the percentage of children who come to the clinic suffering from gastrointestinal symptoms? What percentage of these children are suffering from functional disorders? I should like to know, in addition, exactly how he explains to the parents the nature of these functional disorders.

DR. WILLIAM A. HAWKE, Toronto: The gastrointestinal tract is probably the most vulnerable to psychic disorders. Does Dr. Griffin agree with me?

DR. J. D. M. GRIFFIN, Toronto: No statistics are available as yet from the Hospital for Sick Children. According to the literature, however, in about 20 to 30 per cent of the children suffering from disturbances of the gastrointestinal tract the disability is functional. Explaining these disturbances to parents is most important. One must explain that there is no organic disease at the root of the trouble, nor is it all due to imagination. Usually they are told a little story. They are asked to imagine sitting down to a lovely dinner and then having the meal suddenly interrupted with a loud noise and the sound of breaking windows. Every one thinks of a serious accident. Every one is frightened, excited and tense. Appetites vanish. Some persons may be nauseated and sick. Yet there is probably no disease of the stomach in any one present. It is easy for the parent to understand this.

I agree with Dr. Hawke's statement that the gastrointestinal tract is one of the body systems most sensitive to emotional stimuli. The circulatory system also commonly reflects emotional changes which cause functional disability.

CUTANEOUS TESTS AND TREATMENT OF PATIENTS WITH ASTHMA. DR. JOHN R. ROSS and DR. J. F. MCCREARY (by invitation), Toronto.

Patients with asthma were divided into two groups. Of 12 control patients given injections of saline solution twice a week for eight months, none showed any improvement. Of 16 patients treated for the same length of time with an extract containing house dust, chicken feathers, dog hair and horse dander, the condition of 6 was markedly improved, of 8 improved and of 2 unimproved, as shown by a reduction in the number and duration of attacks.

Eleven additional patients were treated for two years continuously, as in the perennial treatment of hay fever, and these have shown similar improvement.

Elimination of environmental allergens was found to be an unsatisfactory method of treatment except in a few instances.

DISCUSSION

DR. D. P. ARNOLD, Buffalo, N. Y.: What was done about the control group? Were they treated later?

DR. JOHN R. ROSS, Toronto: We are planning to treat them later.

BIOPHOTOMETER IN TESTING VITAMIN A DEFICIENCY. DR. CHARLES E. SNELLING, Toronto.

The biophotometer described by Jeans, Blanchard and Zentmire was used to study the dark adaptation of a group of Toronto school children during the past year. The exact technic and standards employed by the authors just mentioned were used. Two tests were made with no addition to the diet. The children were then given 13,000 units of vitamin A in the form of a preparation containing 50 per cent percomorph liver oil daily for three weeks, and a third test was done. The oil was continued for a second three week period, and a fourth test was done. The results lacked consistency, and there was no evidence of improvement after the large doses of vitamin A. In conclusion, we have found that for children the biophotometer is unsatisfactory as a method of estimation of variations in dark adaptation such as might be produced by vitamin A deficiency.

DISCUSSION

DR. S. GRAHAM ROSS, Montreal: Did any of the patients clinically show night blindness?

DR. CHARLES E. SNELLING, Toronto: Of the group reported here, none was known to have clinical night blindness. Of the group of children that I tested with the Birch-Hirschfeld instrument, 1 or 2 were unable to see things in a dark room. Some patients with retinitis pigmentosa were also tested, but they are not included in this group.

PREVENTION OF WHOOPING COUGH. DR. NELLES SILVERTHORNE, Toronto.

By the use of the cough plate a diagnosis of whooping cough can be made in a high percentage of cases before the appearance of the whoop.

A whooping cough vaccine made from recently isolated strains has been tested for its protective effect in animals and has also proved efficacious in immunizing children against the disease.

DISCUSSION

DR. E. A. MORGAN, Toronto: Will the vaccine prepared by the Department of Health protect mice?

DR. H. M. KEITH, Montreal: Dr. Silverthorne has reported his results in almost the same words as Dr. Sauer. Has he used Sauer's vaccine?

DR. S. J. USHER, Montreal: Does he feel that three weeks or four weeks of treatment is better?

DR. NELLES SILVERTHORNE, Toronto: The vaccine of the Department of Public Health protects mice. I do not know how long this laboratory subcultures these strains. That they protect mice does not mean that they produce as good an antigen as those that have not been subcultured so many times. My associates and I feel that with our vaccine, which is subcultured only five times, we possibly avoid any loss of antigenic potency, such as might occur as the result of more frequent subcultures. In the early stages of our research, some of the children were inoculated with vaccine sent to us by Dr. Sauer. His vaccine also is made from recently isolated strains.

With reference to Dr. Usher's question, we prefer four weeks of treatment with 1 cc. injected into each arm. We obtained some rather undesirable reactions with amounts of over 1 cc. It simplifies the treatment to inject 1 cc. into each arm for four weeks. Since we have followed this procedure, there have been no serious reactions.

SUBDURAL EFFUSION IN AN INFANT ASSOCIATED WITH NONDIABETIC GLYCOSURIA, DIABETES INSIPIDUS AND ALBUMINURIA. DR. S. GRAHAM ROSS and DR. W. V. CONE (by invitation), Montreal.

An infant at the age of 9 months had polydipsia, polyuria, glycosuria and albuminuria. The child had previously been healthy, and there was no history of an injury to the head.

Examination showed that the infant was suffering from a nondiabetic type of glycosuria. Apart from the albuminuria, there was no evidence of renal disease. Although a tentative diagnosis of renal glycosuria was made, the presence of polyuria, of unexplained periods of fever and of vomiting suggested a cerebral lesion. An encephalogram revealed the presence of bilateral subdural effusion associated with marked cerebral atrophy and communicating hydrocephalus. The origin of this was probably traumatic. The subdural spaces were drained through openings in the parietal bones. The fluid was xanthochromatic and had a high protein content, which is typical of subdural effusions. The intake of fluid and output of urine were of the order seen in cases of diabetes insipidus. There are grounds for the hypothesis that the diabetes insipidus, albuminuria and fever were due to a lesion of the hypothalamus, resulting from the subdural effusion and consequent increase of intracranial pressure. The glycosuria was probably also of cerebral origin, although most types of cerebral lesion, such as pituitary lesions and experimental glycosuria due to piqûre (Claude Bernard), are of the diabetic type and are associated with hyperglycemia. No attempt is made to explain the mechanism of the glycosuria in this patient. The infant has survived; but his physical and his mental development are retarded, and the diabetes insipidus, glycosuria and albuminuria persist.

DISCUSSION

DR. H. M. KEITH, Montreal: What was the spinal fluid pressure?

DR. S. ROSS GRAHAM, Montreal: The spinal fluid pressure was normal, but the subdural pressure was increased.

Book Reviews

Orthopädie und Kinderlähmung. By Dr. Friedrich Mommsen. Price, 3.8 marks. Pp. 59, with 36 illustrations. Stuttgart: Ferdinand Enke, 1938.

The normal muscles and their innervation enable one to go about one's work. If there is a disturbance in the innervation of the muscles, accessory muscles must take on the work of those which are handicapped. It is in this type of trouble that the orthopedic surgeon's assistance is required.

A tendency to the development of contractures is due to the loss of muscular balance. Although there may be no demonstrable paralysis, there may be a little weakness, with a tendency for contractures to develop. There is a predilection for involvement of the extensor muscles, with resulting flexion deformities. The state of flexion is the state of relaxation, which gives the patient less pain. When certain muscles are paralyzed and the contractures have developed, the situation is unfavorable for correction because of associated structural changes in the bones and joints.

In the treatment of contractures, Dr. Mommsen is opposed to the sudden correction by an operative measure, such as tenotomy, and rather prefers to correct the deformity by gradually increasing the traction by mechanical means. However, if the correction cannot be gained thus the last 20 degrees of correction may be obtained by partial tenotomy or by section of the associated tendons in the contracture. The amount of correction of a flexed knee is determined by the position of the skeletal portion of the foot.

In the prophylaxis and treatment of deformities of the foot, Dr. Mommsen believes that good position must be maintained for a long time by splints or foot plates. After deformities have developed he prefers redressment by an osteoclast. Only for an extreme condition, such as talipes cavus, does he consider the bloody operation indicated. Even then he prefers redressment first and retention of the correction for some time, to allow the muscles to regain their function. If they should not, after the conservative treatment, then one may consider tenotomies of the plantar fascia and of the calcaneocuboid ligaments or other plastic operation on tendons.

Examination of young children for paralysis is difficult; it is usually done by the pinprick of the skin. In older children electrical stimulation is used. When there is paralysis of groups of muscles the entire picture must be considered. The profession of the patient must be taken into account in outlining the treatment. For example, certain procedures should be emphasized if the person must use the limbs for walking or standing, while other procedures are indicated if he has a sedentary occupation.

Cooperation of the orthopedic surgeon is needed, as in giving gymnastic and electric treatment after the acute stage of the condition. Light and gradual extension exercises are used. Gymnastic exercise is to be regulated according to the position of the limb, i. e., dangling or acutely flexed, the latter position requiring more effort. The galvanic treatment is preferred to the faradic. Fatigue is avoided by treating one muscle for a while and then treating other muscles before stimulating the first again.

Orthopedic apparatus should supply gradual pressure to prevent deformities, as with gradual elevation of the mattress (as an inclined plane) in returning the patient to the standing position. Splints, springs and adhesive fixation are also used. With paralysis about the hip, the use of countersupports on the normal limb is desirable; in this way strain on the weakened muscles is avoided, and hence there are less danger of fatigue and less tendency to the development of deformities about the involved hip.

As to operative treatment, the age for tendon graft should be at least 6 years and that for arthrodesis 8 to 10 years. In tendon graft the deformities should be corrected first. The sheath of the tendon should be transplanted with the tendon if the procedure is to be most efficient.

For the education of the individual grafted tendon, passive motion is used from the fifth day on and active motion later. Local faradic stimulation to the individual transplanted muscle is indicated, as is the protection of the transplant by apparatus or by splints till it is determined that the function of the transplant is satisfactory.

The restoration of the person to his place is valuable to society, as well as psychically beneficial to the patient.

Die offene Lungentuberkulose bei Kindern und Jugendlichen. By Dr. Kurt Klare and Dr. Frieda Böhnung. Price, paper, 13.50 marks; bound, 15 marks. Pp. 164, with 91 illustrations and 23 tables. Leipzig: Georg Thieme, 1938.

This monograph advances the novel concept that the prognosis of open tuberculosis depends on the constitutional type of the individual patient. The term "constitutional type" is defined by the authors as an inherited, unalterable state of reactivity to exogenous and endogenous stimuli. After reviewing and analyzing the case material in their institution from 1916 to 1936, they conclude that the child with open tuberculosis who is of the exudative-lymphatic constitutional type has the best prognosis. The following criteria were employed in placing a child in this category:

1. A history of frequent illnesses of inflammatory nature, especially a tendency to infections of the throat
2. Light hair and light eyes
3. A hyperactive skin, as evidenced by dermographism and a marked tuberculin reaction
4. Enlarged cervical lymph nodes
5. Enlarged tonsils

In the monograph entitled "Anaemia of Infancy and Early Childhood" (Medicine **15**:307 [Sept.] 1936) Hugh W. Josephs, discussing "constitution," states on page 310: "A conception as vague as this is not very useful and is likely to be applied too readily to anything not well understood. As knowledge increases, however, not only may we find that many things attributed to differences in individual make-up are actually the result of extrinsic factors at present little more than suspected, but also we shall be able to define this phase of 'constitution' in terms of the processes involved."

I believe that this quotation is eminently applicable to the monograph of Klare and Böhnung.

Les Dessanglées du périnée. By J. D. Mouchotte and L. Chauvois. Price, 60 francs. Pp. 198, with 64 illustrations and 12 colored plates. Paris: L'Expansion Scientifique Française, 1938.

This little monograph is a brief consideration of the management of injuries of the perineum. The first part of the book is devoted to a consideration of pelvic anatomy; this is followed by a discussion of the mechanism of uterine support. A concise discussion of the various types of injury of the pelvic floor and of the uterine supports is followed by a description of the symptoms of injuries of these structures. It is emphasized that extensive damage to the pelvic supporting structures can be prevented by intelligent obstetric care. The last part of the volume is devoted to treatment of perineal injuries. The authors deal clearly with this part of the subject, and a good idea of the operative methods in use in the French clinics is given. With most of the technic described one may agree. The use of pessaries is well dealt with. This is a subject which of late years has not received sufficient attention, for with the widespread interest in operative procedures the

less spectacular phases of gynecology have been somewhat neglected. The pessary, as the authors justly recognize, has a limited but real field of usefulness. The treatment of prolapse, except that using various types of supports, is not dealt with. A number of the illustrations are of the anaglyph type, requiring the use of colored pieces of celluloid in a pasteboard holder for their clear visualization. These are not altogether satisfactory. The remainder of the illustrations are drawings, which are much better. This book presents a good review of the essential facts concerning perineal injuries.

Die postvaccinale Encephalitis. By Marius Kaiser and Julius Zappert. Price, 4.80 marks. Pp. 97, with 3 tables. Vienna: Julius Springer, 1938.

In compiling and evaluating data on encephalitis following vaccination for smallpox, the authors have accomplished a commendable task. Though the origin of the disease remains a mystery, any effort toward classifying its known factors constitutes a step toward better understanding. The disease is properly treated as an entity, with a description befitting its clinical implications. The symptomatology, the pathology and the course of this strange condition are excellently covered. Unfortunately, the discussion of the therapy is devoid of any specific facts. This shortcoming, however, is not in any way attributable to oversight on the part of the authors. For how can the prophylaxis be described efficiently when the etiology is so ill understood? How can treatment be complete when many contributing factors associated with the disease are hidden in obscurity?

The monograph is nevertheless rich in content, especially in statistical material. The clinical descriptions are profusely illustrated with cases typifying the various phases of the disease. It is indeed a most valuable little volume, and it is certain to maintain the interest of neurologist and pediatrician alike.

The Chemistry of Antigens and Antibodies. By J. R. Marrack. Price, 3s. net. Pp. 194, with *27* illustrations and *26* tables. London: His Majesty's Stationery Office, 1938.

This monograph is an extensively revised edition of Special Report 194, which was published by the British Medical Research Council in 1934 as a guide to future workers on the chemical nature of the phenomena associated with immunity to infection. There are 194 pages and six chapters dealing with physicochemical considerations (including molecular size, polar forces, structure of proteins and stability of suspensions), the nature of antibodies, the specificity of antigens and the nature of antigen-antibody reactions, in both the first and the second stage. The author has presented the latest knowledge in this particular field of immunity in a thorough and scholarly manner.

CORRECTION

In the review of "The Treatment of Clinical and Laboratory Data: An Introduction to Statistical Ideas and Methods for Medical and Dental Workers," by Dr. Donald Mainland, which appeared in the September issue (AM. J. DIS. CHILD. **56**:713, 1938), the price was given as $15 instead of 15 shillings.

Directory of Pediatric Societies*

INTERNATIONAL

International Association of Preventive Pediatrics

President: Prof. S. Monrad, Dronning Louises Børnehospital, Copenhagen, Denmark.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

International Congress of Pediatrics

President: Prof. Luigi Spolverini, Policlinico Lungo Tevere Melini 24, Rome, Italy.
Secretary: Professor Vitetti, Rome, Italy.
Place: Boston. Time: Sept. 9-12, 1940.
American Committee:
Chairman: Dr. Henry F. Helmholz, Mayo Clinic, Rochester, Minn.
Secretary: Kenneth Blackfan, 300 Longwood Ave., Boston.
Canadian Committee:
Chairman: Dr. Alan Brown, Hospital for Sick Children, 67 College St., Toronto.
Secretary: Dr. H. P. Wright, 1509 Sherbrooke St., W., Montreal.

International Congress for the Protection of Infancy

Secretary: Prof. G. B. Allaria, Corso Bramante 29, Torino 120, Italy.

FOREIGN

British Paediatric Association

President: Dr. Hector C. Cameron, 23 Devonshire Pl., Upper Wimpole St., London, W. 1.
Secretary: Dr. Arthur G. Maitland Jones, 31A Weymouth St., London, W. 1.

Danish Pediatric Society

President: Dr. E. Lenstrup, Copenhagen.
Secretary: Dr. E. Gjørup, Dronning Louises Børnehospital, Copenhagen.

Paediatrický Spolok na Slovensku

President: Dr. A. J. C. Chura, Lazaretská 11, Bratislava.
Secretary: Dr. P. Rados, Lazaretská 6, Bratislava.
Place: Pediatric Clinic, University Bratislava. Time: Six times a year.

Royal Society of Medicine, Section for the Study of Disease in Children

President: Dr. E. A. Cockayne, 98 Harley St., London, W. 1, England.
Secretary: Dr. R. Lightwood, 86 Brook St., London, W. 1, England.
Place: 1 Wimpole St., London. Time: Fourth Friday of each month, 4:15 p. m.

Palestine Jewish Medical Association, Section of Physicians of Children's Diseases

President: Prof. S. Rosenbaum, 26 Bialikstr., Tel Aviv.
Secretary: Dr. A. Brünn, 9 Maazestre, Tel Aviv.

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* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

Sociedad Cubana de Pediatría

President: Dr. Clemente Inclan Costa, Manrique 48, Habana.
Secretary: Dr. Serafin Falcon Lopez, Calle B No. 356, Vedado, Habana.
Place: Cátedra de Clinica Infantil, Hospital Mercedes, Habana. Time: Last Wednesday of every month.

Société de Pédiatrie de Paris

President: Dr. B. Weill-Hallé, 49 Avenue Raymond Poincaré, Paris, France.
Secretary: Dr. Jean Hallé, 10 bis Rue du Pré aux Clercs, Paris, France.
Place: Hôpital des Enfants Malades, 49 Rue de Sèvres. Time: 4:30 p. m., third Thursday of every month.

NATIONAL

American Medical Association, Scientific Assembly, Section on Pediatrics

Chairman: Dr. Edward Clay Mitchell, 1073 Madison Ave., Memphis, Tenn.
Secretary: Dr. Albert D. Kaiser, 16 N. Goodman St., Rochester, N. Y.
Place: Hotel Chase, St. Louis. Time: May 15-19, 1939.

American Academy of Pediatrics

President: Dr. H. F. Helmholz, Mayo Clinic, Rochester, Minn.
Secretary: Dr. C. G. Grulee, 636 Church St., Evanston, Ill.
Place: Netherland Plaza Hotel, Cincinnati. Time: Nov. 16-18, 1939.
Region I. Place: Waldorf-Astoria Hotel, New York. Time: June 1-3, 1939.
Region II. Place: Skirven Hotel, Oklahoma City. Time: Nov. 16, 1938.

American Hospital Association, Children's Hospital Section

Chairman: Miss Mabel Binner, Children's Memorial Hospital, Chicago.
Secretary: Winifred Culbertson, Children's Convalescent Hospital, Cincinnati.

American Pediatric Society

President: Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid St., St. Louis.
Place: Skytop Lodge, Skytop, Pa. Time: April 27-29, 1939.

Canadian Society for the Study of Diseases of Children

President: Dr. R. R. MacGregor, 142 Wellington St., Kingston, Ontario.
Secretary-Treasurer: Dr. Elizabeth Chant Robertson, Hospital for Sick Children, Toronto.

Society for Pediatric Research

President: Dr. L. Emmett Holt Jr., Johns Hopkins Hospital, Baltimore.
Secretary: Dr. A. A. Weech, 3975 Broadway, New York.

SECTIONAL

North Pacific Pediatric Society

President: Frederick Fischer, 407 Riverside Ave., Spokane, Wash.
Secretary: Dr. C. L. Lyons, Paulsen Medical-Dental Bldg., Spokane, Wash.

Southern Medical Association, Section of Pediatrics

Chairman: Dr. Charles E. Conrad, 209-210 Professional Bldg., Harrisburg, Va.
Secretary: Dr. Hughes Kennedy Jr., Highland Plaza Apts., Birmingham, Ala.
Place: Oklahoma City. Time: Nov. 15-18, 1938.

STATE

Alabama Pediatric Society

President: Dr. Stewart H. Welch, 1117 S. 20th St., Birmingham.
Secretary-Treasurer: Dr. William R. Britton, 4 Catoma St., Montgomery.
Place: Montgomery. Time: April 17, 1939.

Arkansas State Pediatric Association

Chairman: Dr. G. D. Murphy, 112 Peach St., El Dorado.
Secretary: Dr. Madeline M. Melson, 909 Main St., Little Rock.
Place: Hot Springs. Time: January 1939.

California State Medical Society, Section on Pediatrics

Chairman: Dr. Harold K. Faber, 2341 Clay St., San Francisco.
Secretary: Dr. Hartzel H. Ray, 23–2d Ave., San Mateo.

Florida State Pediatric Society

President: Dr. Gilbert S. Osincup, 300 E. Colonial Dr., Orlando.
Secretary: Dr. Warren W. Quillian, 227 Avenue Aragon, Coral Gables.
Place: Concurrent with state association meeting at time of convention.

Georgia Pediatric Society

President: Dr. Charles Hall Farmer, 553 Walnut St., Macon.
Secretary-Treasurer: Dr. Don F. Cathcart, 478 Peachtree St., N. E., Atlanta.
Scientific Meeting—Place: Augusta. Time: December 1938.
Business Meeting—Place: Atlanta. Time: April 1939.

Hezekiah Beardsley Pediatric Club of Connecticut

President: Dr. C. V. Calvin, 144 Golden Hill St., Bridgeport.
Secretary: Dr. E. T. Wakeman, 129 Whitney Ave., New Haven.
Time: Three meetings a year.

Indiana State Pediatric Society

President: Dr. O. N. Torian, 23 E. Ohio St., Indianapolis.
Secretary-Treasurer: Dr. Mathew Winters, 621 Hume Mansur Bldg., Indianapolis.
Time: Two meetings a year.

Iowa Pediatric Society

President: Dr. Morgan J. Foster, 837 Higley Bldg., Cedar Rapids.
Secretary-Treasurer: Dr. Arnold M. Smythe, 406–6th Ave., Des Moines.

Louisiana State Pediatric Society

President: Dr. Ruth Aleman, 1407 S. Carrollton Ave., New Orleans.
Secretary-Treasurer: Dr. Philip C. de Verges, 312 Audubon Bldg., New Orleans.

Medical Society of State of New York, Section on Pediatrics

Chairman: Dr. Paul W. Beaven, 26 S. Goodman St., Rochester.
Secretary: Dr. Leslie O. Ashton, 842 Park Ave., New York.

Medical Society of the State of Pennsylvania, Pediatric Section

Chairman: Dr. John P. Scott, 1740 Bainbridge St., Philadelphia.
Secretary: Dr. John M. Higgins, 600 S. Wilbur Ave., Sayre.

Michigan State Medical Society, Pediatric Section

Chairman: Dr. Allan L. Richardson, 3001 W. Grand Blvd., Detroit.
Secretary: Dr. Ward L. Chadwick, 524 Medical Arts Bldg., Grand Rapids.

Mississippi State Pediatric Society

President: Dr. Guy C. Jarratt, 920 Crawford St., Vicksburg.
Secretary-Treasurer: Dr. Harvey F. Garrison Jr., 315 E. Capitol Pl., Jackson.
Place: To be designated by society. Time: Yearly.

Nebraska Pediatric Society

President: Dr. Herman M. Jahr, 1120 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. Elmer W. Bantin, 440 Aquila Court Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

North Carolina Pediatric Society

President: Dr. W. Myers Hunter, 306 N. Tryon St., Charlotte.
Secretary: Dr. J. R. Adams, 412 N. Church St., Charlotte.

Oklahoma State Pediatric Society

President: Dr. A. L. Salomon, 1200 N. Walker St., Oklahoma City.
Secretary: Dr. Ben H. Nicholson, 301 W. 12th St., Oklahoma City.

South Carolina Pediatric Society

President: Dr. Mylnor W. Beach, 126 Meeting St., Charleston.
Secretary-Treasurer: Dr. D. Lesesne Smith Jr., 187 Oakland Ave., Spartanburg.

Tennessee State Pediatric Society

President: Dr. William E. Van Order, 546 McCallie Ave., Chattanooga.
Secretary: Dr. Kinsey M. Buck, 1193 Madison Ave., Memphis.
Place: Jackson. Time: April 11, 1939.

Texas Pediatric Society

President: Dr. F. O. Calaway, 3306 Fannin St., Houston.
Secretary-Treasurer: Dr. F. H. Lancaster, 4409 Fannin St., Houston.
Place: Houston. Time: May 9, 1939.

Virginia Pediatric Society

President: Dr. W. Ambrose McGee, 616 W. Grace St., Richmond.
Secretary: Dr. John M. Bishop, Medical Arts Bldg., Roanoke.

West Virginia State Medical Society, Section on Pediatrics

President: Dr. J. L. Blanton, 207 Fairmont Ave., Fairmont.
Secretary: Dr. Theresa O. Snaith, 450 Center Ave., Weston.

LOCAL

Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. N. C. Wetzel, 2103 Adelbert Rd., Cleveland.
Secretary: Dr. Fred Rittenger, 10515 Carnegie Ave., Cleveland.
Place: Cleveland Medical Library Bldg. Time: October, December, February and April.

Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. T. B. Verner, 170 St. George St., Toronto, Canada.
Secretary: Dr. D. V. Hutton, 170 St. George St., Toronto, Canada.

Bronx Pediatric Society

President: Dr. Samuel Tripler, 1555 Grand Concourse, New York.
Secretary: Dr. Harry S. Altman, 940 Grand Concourse, New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Every second Wednesday of each month, except June, July, August and September.

Brooklyn Academy of Pediatrics

President: Dr. Benjamin Kramer, 6 Pierrepont St., Brooklyn.
Secretary: Dr. John A. Monfort, 861 Carroll St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Fourth Wednesday of each month, except May, June, July, August and September.

Central New York Pediatric Club

President: Dr. Frank Vasder Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Third Thursday of April and September.

Chicago Pediatric Society

President: Dr. Joseph K. Calvin, 2376 E. 71st St., Chicago.
Secretary: Dr. George F. Munns, 723 Elm St., Winnetka, Ill.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month, October to May, inclusive.

Dallas Pediatric Society

President: Dr. W. H. Bradford, 1719 Pacific Ave., Dallas, Texas.
Secretary-Treasurer: Dr. John E. Ashby, 3622 Fairmont Ave., Dallas, Texas.
Place: Bradford Baby Hospital. Time: 1 p. m., second and fourth Saturdays of each month.

Detroit Pediatric Society

President: Dr. William O'Donnell, 1553 Woodward Ave., Detroit.
Secretary: Dr. Robert Mason, 5140 Second Blvd., Detroit.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month from October to June, inclusive.

Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. L. H. Goldsmith, 384 Peachtree St., N. E., Atlanta.
Secretary: Dr. James P. Hanner, 384 Peachtree St., N. E., Atlanta.
Place: Academy of Medicine, 38 Prescott St., N. E. Time: Second Thursday of each month from October to April, 8 p. m.

Houston Pediatric Society

President: Dr. John K. Glen, 4412 Montrose Blvd., Houston, Texas.
Secretary-Treasurer: Dr. J. L. Collier, 1620 Medical Arts Bldg., Houston, Texas.
Place: Houston Club. Time: Third Monday of each month.

Intermountain Pediatric Society

President: Dr. Eugene Smith, 385–24th St., Ogden, Utah.
Secretary-Treasurer: Dr. W. C. Cheney, 837 Boston Bldg., Salt Lake City.
Place: Salt Lake City General Hospital. Time: First Thursday of each month, 8 p. m.

Kansas City (Missouri) Pediatric Society

President: Dr. Urban Busiek, 200 E. Pershing St., Springfield, Mo.
Secretary: Dr. Fred Speer, 2700 Parallel Ave., Kansas City, Kan.
Place: Kansas City General Hospital. Time: On call.

Los Angeles County Medical Association, Pediatric Section

President: Dr. H. R. Cooder, 3875 Wilshire Blvd., Los Angeles.
Secretary-Treasurer: Dr. Paul M. Hamilton, 248 E. Main St., Alhambra, Calif.
Place: Los Angeles County Medical Headquarters, 1925 Wilshire Blvd.
Time: Second Monday of February, April, June, October and December.

Medical Society of the County of Kings and the Academy of Medicine of Brooklyn, Pediatric Section

President: Dr. Sidney D. Kramer, 61 Eastern Parkway, Brooklyn.
Secretary: Dr. Benjamin Stoloff, 1149 Eastern Parkway, Brooklyn.
Place: 1313 Bedford Ave., Brooklyn. Time: Third Wednesday of each month, October to May.

Medical Society of the County of Queens, Inc., Section on Pediatrics

Chairman: Dr. James Dobbins, 42-04 Ditmars Blvd., Long Island City, N. Y.
Secretary-Treasurer: Dr. Edith A. Mittell, 144–38th Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

Memphis Pediatric Society

President: Dr. Barton Etter, 376 S. Bellevue St., Memphis, Tenn.
Secretary-Treasurer: Dr. Harry Jacobson, 1193 Madison Ave., Memphis, Tenn.
Place: John Gaston Hospital. Time: Quarterly.

Milwaukee Pediatric Society

President: Dr. Joseph Shimpa, 2309 N. 36th St., Milwaukee.
Secretary: Dr. Helen Jane Zillmer, 781 N. Jefferson St., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

New England Pediatric Society

President: Dr. Hyman Green, 483 Beacon St., Boston.
Secretary-Treasurer: Dr. Henry E. Gallup, 1101 Beacon St., Brookline, Mass.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Philip M. Stimson, 25 Claremont Ave., New York.
Secretary: Dr. Lucy Porter Sutton, 168 E. 74th St., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

Northwestern Pediatric Society

President: Dr. Robert Rosenthal, 437 Lowry Medical Arts Bldg., St. Paul.
Secretary-Treasurer: Dr. R. E. Nutting, 205 W. 2d St., Duluth, Minn.
Place: Minneapolis, St. Paul, Duluth and Rochester. Time: January, April, July and October.

Oklahoma City Pediatric Society

President: Dr. A. L. Salomon, 1200 N. Walker St., Oklahoma City.
Secretary: Dr. G. R. Felts, 1200 N. Walker St., Oklahoma City.
Time: Every month, except June, July and August.

Philadelphia Pediatric Society

President: Dr. Julian M. Lyon, 40 Llanfair Rd., Ardmore, Pa.
Secretary: Dr. Aims C. McGuinness, Children's Hospital, 1740 Bainbridge St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to April, inclusive.

Pittsburgh Pediatric Society

President: Dr. James LeRoy Foster, Highland Bldg., Pittsburgh.
Secretary-Treasurer: Dr. E. R. McClusky, 3200–5th Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months from October to June, inclusive.

Richmond Pediatric Society

President: Dr. A. S. Hurt, 1028 W. Franklin St., Richmond, Va.
Secretary-Treasurer: Dr. Louise Fry Galvin, 2416 Stuart Ave., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: First Thursday of each month, except July, August and September.

Rochester Pediatric Society

President: Dr. J. Merrel Parker, 11 N. Goodman St., Rochester, N. Y.
Secretary: Dr. H. C. Soule, 16 N. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: Second Friday of each month.

Rocky Mountain Pediatric Society

President: Dr. John Schoonover, Republic Bldg., Denver.
Secretary: Dr. F. Craig Johnson, 1850 Gilpin St., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 7:30 p. m.

St. Louis Pediatric Society

President: Dr. John Zahorsky, 536 N. Taylor Ave., St. Louis.
Secretary-Treasurer: Dr. Max Deutch, 634 N. Grand Blvd., St. Louis.
Place: St. Louis Medical Society. Time: Third Friday of every month.

Seattle Pediatric Society

President: Dr. Jay I. Durand, 1305–4th Ave., Seattle.
Secretary: Dr. Frederick B. Joy, 1215–4th Ave., Seattle.
Place: College Club. Time: Third Friday of each month, 6:30 p. m.

Southwestern Pediatric Society

President: Dr. Philip E. Rothman, 3875 Wilshire Blvd., Los Angeles.
Secretary: Dr. Norman Nixon, 1136 W. 6th St., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. Damon O. Walthall, 1103 Grand Ave., Kansas City, Mo.
Secretary: Dr. D. Murray Cowie, University of Michigan, Ann Arbor, Mich.
Place: Horace H. Rackham Graduate School, Ann Arbor, Mich. Time: Nov. 11-12, 1938.

Westchester County Medical Society, Pediatric Section (New York)

President: Dr. Norman Survis, 650 Main St., New Rochelle.
Secretary-Treasurer: Dr. Elvira Ostlund, 131 Purchase St., Rye.
Place: Grasslands Hospital, Valhalla, N. Y. Time: Third Thursday in October, December, February and April.